



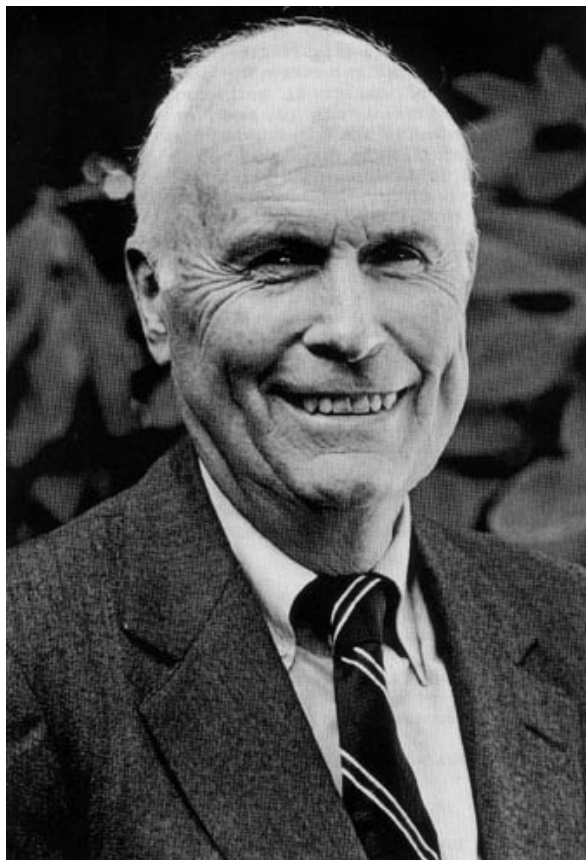
*Program in the History of the Biological Sciences and Biotechnology*

**Stanford's Office of Technology Licensing and the Cohen/Boyer  
Cloning Patents**

**Niels Reimers**

*Interviews Conducted by  
Sally Smith Hughes, Ph.D.  
in 1997*

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**Niels Reimers, 1996. Photograph by Michele Firpo.**

## **Introductory Materials**

### **Legal Information**

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

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It is recommended that this oral history be cited as follows:

Niels Reimers, "Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents," an oral history conducted in 1997 by Sally Smith Hughes, Ph.D., Regional Oral History Office, The Bancroft Library, University of California, Berkeley, 1998.

## Abstract

Reimers, Niels(b. 1933), University Technology Licensing Officer

*Stanford's Office of Technology Licensing and the Cohen/Boyer Cloning Patents*, 1998, ix, 84 pp.

Pre-Stanford career in industry; establishing a technology licensing program at Stanford University; Cohen-Boyer recombinant DNA patents: negotiating with inventors, Stanford, and University of California, and commercial potential, royalty distribution, controversy over patenting in biology, licensing plan, recombinant DNA controversy, National Institutes of Health role, opening patent files to public, Chakrabarty Supreme Court case, claims by John Morrow and Robert Helling; patenting and licensing monoclonal antibodies; Pajaro Dunes Conference on Biotechnology, 1982; University Licensing Pool for Technology (ULab); comments on Stanley Cohen, Herbert Boyer, and Donald Kennedy.

Interviewed 1997 by Sally Smith Hughes, Ph.D., for the Program in the History of the Biological Sciences and Biotechnology, Regional Oral History Office, The Bancroft Library, University of California, Berkeley.

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## Interview History

This short oral history with Niels Reimers focuses on only one, albeit a major, aspect of his career in technology licensing at Stanford University: his pursuit of the patenting and licensing of recombinant DNA cloning technology devised by Stanley Cohen of Stanford and Herbert Boyer of the University of California, San Francisco. The three patents are basic tools of biotechnology, licensed by every company engaged in recombinant DNA science and bringing immense royalty income to the two universities.

The discussion begins with Reimers' arrival at Stanford in 1968 as associate director of the Sponsored Projects Office. Soon after, he initiated a pilot program promoting the patenting and licensing of Stanford faculty "inventions" thought to have commercial application. Immediately successful in increasing the university's patent income, the program was formally established in 1969 as Stanford's Office of Technology Licensing [OTL], with Reimers as director. The campus had thus acquired an efficient mechanism to facilitate "technology transfer"--the catch phrase for the process in which information embodied in basic science discoveries is transferred to industry for commercial development. The essence of this process is patenting and licensing--patenting by the U.S. Patent and Trademark Office [PTO] in Washington, D.C., and licensing, in this case by Stanford's OTL, to companies of the right to use the patented "technology".

Reimers tells in the oral history how he learned in the spring of 1974 that Cohen and Boyer had developed a technique for joining DNA segments from different sources and replicating or "cloning" them in bacteria--recombinant DNA technology, as it came to be known. Reimers contacted Cohen, who confirmed that the technique had commercial as well as scientific potential. Thus began a long and arduous process, lasting well over a decade, of attempting first to patent and then to license the Cohen-Boyer process and products.

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Reimers describes how he submitted a patent application in late 1974 shortly before the patent "bar", the one-year period after "disclosure" or communication of the discovery, within which a patent application must be filed according to U.S. patent law. The process was far from straightforward. University biologists up to this point had by and large stuck to "pure" basic research. Commercial application of academic research was largely confined to their colleagues in engineering, chemistry, and other applied fields. Although patenting in medicine was not unknown--the University of Toronto's patent on insulin is an early example--academia nonetheless approached commercialization of discoveries in biomedicine warily and usually sought means to avoid direct involvement. OTL's direct and aggressive management of the patenting and licensing of DNA cloning technology was a new departure.

There were other stumbling blocks to patenting and licensing the Cohen-Boyer work. The period between 1974 to 1980, when Reimers and others were negotiating with the PTO to issue the first of the three recombinant DNA patents, was a time of heightened concern about the safety of recombinant DNA science. Paul Berg, the leading scientist in the recombinant DNA biohazard debate, was also at Stanford and outspoken in his belief that the university's patenting effort would undercut his position as primary spokesman for the resumption of research under government guidelines. For this and other reasons, Reimers and other Stanford officials trod softly during the 1970s when the patents were pending.

By the late 1970s, there was another problem stalling Stanford's effort to patent the Cohen-Boyer procedure: the Supreme Court was considering the patenting of "life forms" in the renowned Chakrabarty case in which General Electric sought to patent an organism constructed to metabolize oil. In view of the legal indecision regarding the patentability of living organisms, Stanford dropped its "product" claim --its claim on recombinant organisms--and

filed a patent application on the cloning process alone. On December 2, 1980, the PTO issued the first Cohen-Boyer patent, the so-called "process" patent.

Reimers recounts his efforts to structure a licensing program which would encourage wide industry utilization of the new technology and, by setting low licensing fees, discourage litigation. After 15 percent had been taken off the top to pay for Stanford's management of the patent, potential royalties were to be split 50-50 between Stanford and UCSF, the university affiliations of Cohen and Boyer. The dissensions of this period and the increasing participation of Stanford administrators, from President Donald Kennedy on down, are outlined in the oral history. In 1984 and 1988, the PTO approved the two "product" patents, on "lower" (prokaryotic) and "higher" (eukaryotic) organisms.

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## The Oral History Process

One interview, somewhat hastily arranged when I learned that Reimers was about to retire, was conducted in his office in the UCSF Faculty Club, where in March 1996 he established the campus's first Office of Technology Management. Down-to-earth and friendly, he attempted to cover a complex period of history in a short time. The result is insightful but not comprehensive. For further research, the interested reader is referred to the extensive records on the Cohen-Boyer patent at Stanford's OTL. Some of these documents were used in the course of the interview and suggest the richness of this collection, as well as their value in getting beyond "an oft-told tale."

There is intrinsic interest in this history of major patents as told by the man most responsible for steering them through the patenting procedure and for creating the structure and terms of the licensing process. His tenacity in this arduous business stemmed in part from his gradual realization of what these patents could mean to the two universities in income and prestige. But the oral history also suggests a dramatic shift in philosophy as university administrators, industry figures, and university scientists learned the value--scientific, commercial, and financial--of discoveries in biological science. Reimers is among those responsible for facilitating the increasingly complex interconnections between the academic and industrial worlds.

The Regional Oral History Office was established in 1954 to augment through tape-recorded memoirs the Library's materials on the history of California and the West. Copies of all interviews are available for research use in The Bancroft Library and in the UCLA Department of Special Collections. The office is under the direction of Willa K. Baum, Division Head, and the administrative direction of Charles B. Faulhaber, James D. Hart Director of The Bancroft Library, University of California, Berkeley.

Sally Smith Hughes, Ph.D. Research Historian/Senior Interviewer

Regional Oral History Office

The Bancroft Library

Berkeley, California

March 1998

## Biotechnology Series History---Sally Smith Hughes, Ph.D.

### Genesis of the Program in the History of the Biological Sciences and Biotechnology

In 1996, a long-held dream of The Bancroft Library came true with the launching of its Program in the History of the Biological Sciences and Biotechnology. For years, Bancroft had wished to document the history of the biological sciences on the Berkeley campus, particularly its contributions to the development of molecular biology. Bancroft has strong holdings in the history of the physical sciences--the papers of E.O. Lawrence, Luis Alvarez, Edwin McMillan, and other campus figures in physics and chemistry, as well as a number of related oral histories. These materials support Berkeley's History of Science faculty, as well as scholars from across the country and around the world.

Although Berkeley is located next to the greatest concentration of biotechnology companies in the world, Bancroft had no coordinated program to document the industry nor its origins in academic biology. For a decade, the staff of the Regional Oral History Office had sought without success to raise funds for an oral history program to record the development of the industry in the San Francisco Bay Area. When Charles Faulhaber arrived in 1995 as Bancroft's new director, he immediately understood the importance of establishing a Bancroft program to capture and preserve the collective memory and papers of university and corporate scientists and the pioneers who created the biotechnology industry. He too saw the importance of documenting the history of a science and industry which influence virtually every field of the life sciences, generate constant public interest and controversy, and raise serious questions of public policy. Preservation of this history was obviously vital for a proper understanding of science and business in the late 20th century.

Bancroft was the ideal location to launch such an historical endeavor. It offered the combination of experienced oral history and archival personnel, and technical resources to execute a coordinated oral history and archival program. It had an established oral history series in the biological sciences, an archival division called the History of Science and Technology Program, and the expertise to develop comprehensive records management plans to safeguard the archives of individuals and businesses making significant contributions to molecular biology and biotechnology. All that was needed was funding.

In April 1996, the dream became reality. An anonymous donor provided seed money for a center at the Bancroft Library for historical research on the biological sciences and biotechnology. Thanks to this generous gift, Bancroft has begun to build an integrated collection of research materials--primarily oral history transcripts, personal papers, and archival collections--related to the history of the biological sciences and biotechnology in university and industry settings. One of the first steps was to create a board composed of distinguished figures in academia and industry who advise on the direction of the oral history and archival components. The Program's initial concentration is on the San Francisco Bay Area and northern California. But its ultimate aim is to document the

growth of molecular biology as an independent field of the life sciences, and the subsequent revolution which established biotechnology as a key contribution of American science and industry.

UCSF Library, with its strong holdings in the biomedical sciences, is a collaborator on the archival portion of the Program. David Farrell, Bancroft's new curator of the History of Science and Technology, serves as liaison. In February 1998, Robin Chandler, head of UCSF Archives and Special Collections, completed a survey of corporate archives at local biotechnology companies and document collections of Berkeley and UCSF faculty in the biomolecular sciences. The ultimate aim is to ensure that personal papers and business archives are collected, cataloged, and made available for scholarly research.

## Project Structure

With the board's advice, Sally Hughes, a science historian at the Regional Oral History Office, began lengthy interviews with Robert Swanson, a co-founder and former CEO of Genentech in South San Francisco; Arthur Kornberg, a Nobel laureate at Stanford; and Paul Berg, also a Stanford Nobel laureate. A short interview was conducted with Niels Reimers of the Stanford and UCSF technology licensing offices. These oral histories build upon ones conducted in the early 1990s, under UCSF or Stanford auspices, with scientists at these two universities.<sup>3</sup> The oral histories offer a factual, contextual, and vivid personal history that enriches the archival collection, adding information that is not usually present in written documents. In turn, the archival collections support and provide depth to the oral history narrations.

## Primary and Secondary Sources

This oral history program both supports and is supported by the written documentary record. Primary and secondary source materials provide necessary information for conducting the interviews and also serve as essential resources for researchers using the oral histories. They also orient scholars unfamiliar with the field or the scientist to key issues and participants. Such orientation is particularly useful to a researcher faced with voluminous, scattered, and unorganized primary sources. This two-way "dialogue" between the documents and the oral histories is essential for valid historical interpretation.

Beginning with the first interviews in 1992, the interviewer has conducted extensive documentary research in both primary and secondary materials. She gratefully acknowledges the generosity of the scientists who have made their personal records available to her: Paul Berg, Stanley Cohen, Arthur Kornberg, William Rutter, Keith Yamamoto. She also thanks the archivists at Bancroft, UCSF, and Stanford libraries, and personnel at Chiron, Genentech, and Stanford's Office of Technology Licensing, for assistance in using archival collections.

## Oral History Process

The oral history methodology used in this program is that of the Regional Oral History office, founded in 1954 and producer of over 1,600 oral histories. The method consists of research in primary and secondary sources; systematic recorded interviews; transcription, light editing by the interviewer, and review and approval by the interviewee; library deposition of bound volumes of transcripts with table of contents, introduction, interview history, and index; cataloging in national on-line library networks (MELVYL, RLIN, and OCLC); and publicity through ROHO news releases and announcements in scientific, medical, and historical journals and newsletters and via the ROHO and UCSF Library web pages.

Oral history as an historical technique has been faulted for its reliance on the vagaries of memory, its distance from the events discussed, and its subjectivity. All three criticisms are valid; hence the necessity for using oral history documents in conjunction with other sources in order to reach a reasonable historical interpretation.<sup>4</sup> Yet these acknowledged weaknesses of oral history, particularly its subjectivity, are also its strength. Often individual perspectives provide information unobtainable through more traditional sources. Oral history in skillful hands provides the context in which events occur--the social, political, economic, and institutional forces which shape the course of events. It also places a personal face on history which not only enlivens past events but also helps to explain how individuals affect historical developments.

An advantage of a series of oral histories on a given topic, in this case molecular biology and biotechnology, is that the information each contains is cumulative and interactive. Through individual accounts, a series can present the complexities and interconnections of the larger picture. Thus the whole (the series) is greater than the sum of its parts (the individual oral histories), and should be considered as a totality.

## Emerging Themes

Although the oral history program is still in its infancy, several themes are emerging. One is "technology transfer," the complicated process by which scientific discovery moves from the university laboratory to industry where it contributes to the manufacture of commercial products. The oral histories show that this trajectory is seldom a linear process, but rather is influenced by institutional and personal relationships, financial and political climate, and so on.

Another theme is the importance of personality in the conduct of science and industry. These oral histories testify to the fact that who you are, what you have and have not achieved, whom you know, and how you relate have repercussions for the success or failure of an enterprise, whether scientific or commercial. Oral history is probably better than any other methodology for documenting these personal dimensions of history. Its vivid descriptions of personalities and events not only make history vital and engaging, but also contribute to an understanding of why circumstances occurred in the manner they did.

Molecular biology and biotechnology are fields with high scientific and commercial stakes. As one might expect, the oral histories reveal the complex interweaving of scientific, business, social, and personal factors shaping these fields. The expectation is that the oral histories will serve as fertile ground for research by present and future scholars interested in any number of different aspects of this rich and fascinating history.

## Location of the Oral Histories

Copies of the oral histories are available at the Bancroft, UCSF, and UCLA libraries. They also may be purchased at cost through ROHO.

Sally Smith Hughes, Ph.D. Research Historian/Senior Interviewer April 1998  
Berkeley, California

## Oral Histories on Molecular Biology and Biotechnology

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

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

In Process

Paul Berg, Ph.D.

Herbert W. Boyer, Ph.D.

Niels Reimers

Robert Swanson

Keith R. Yamamoto, Ph.D.

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— [Date of Interview: May 8, 1997] —

## 1. I: Director, Office of Technology and Licensing, Stanford, 1968-1996

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### Pre-Stanford Career

#### Hughes

Mr. Reimers, please give me a thumbnail sketch of how you ended up at the Office of Technology Licensing [OTL] at Stanford.

#### Reimers

I had been in industry before then, namely at Ampex Corporation [Redwood City, California, 1959-1962] and Philco Western Development Laboratories [Palo Alto, California], which became Philco-Ford Corporation, which then became Ford Aerospace [1963-1968] and is now Loral Corporation. I went from engineering to become a division manager of contracts for Ford. From there I wanted to apply my knowledge in a university setting. I contacted Stanford and was hired by Stanford [May 1968].

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### Establishing a Technology Licensing Program at Stanford

#### Reimers

I soon found out that the business of managing grants and contracts in a university was nowhere near as interesting as at a company. So when a technology disclosure came by, after I had been at Stanford a couple of months, I asked, "What do you do with this?" And they said, "Well, you send it to the Research Corporation, which is based in New York City. They handle inventions for a great number of universities. Then after a few months, they'll respond, and then you take it from there."

I looked up the income we had from Research Corporation from '54 through '67, and it was something like \$4,500. I thought we could do a lot better licensing directly, so I proposed a technology licensing program. And I had some advice: in the university setting, you don't just start a program; you begin a pilot program. So I started it as a pilot program, and proposed how the royalties would be distributed, how the financial structure would be, and began the program later in 1968 on a pilot basis. But I still had my responsibility in the Sponsored Projects Office, so this was a part-time thing.

In that first partial year, the program brought in about \$55,000, and I was making thirteen or fourteen thousand at the time. So Stanford really never had to look back. We were making money from the beginning. And then we set the program up on a formal basis for the next year. After I put together the plan for it, Stanford planned to go out and hire somebody, and I could get back to doing what they hired me for. I said, "Not a chance. I want to do this." And I went to my boss, Ken Creighton, Stanford's controller, who said, "Well, there's not a career path in university administration for this sort of thing. This could be a dead end." My response was, "If I can see my way clear to doing something I've really enjoyed for five years, that's a lifetime."

The next year I raised around seventy-five thousand in royalty income. I thought with a growth in revenue of 50 percent a year, we're going to really do great. But then I had the first downturn in royalty income in the third year, down to seventy-one thousand. But after that third year, we then increased steadily. It's now around forty or so million dollars. I don't know the exact number though.<sup>2</sup>

Typically, a faculty member or a graduate student or research staff member at Stanford sends in an invention disclosure to begin the licensing process. When I started, the volume was probably around twenty-two, twenty-five or so disclosures per year. Very quickly, after we had our own campus program, it built up to fifty-sixty, and then rose, in the last ten or fifteen years, to about one hundred seventy-five a year. Three or four discoveries come in every week. The office manages the licensing of those discoveries.

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## The Cohen-Boyer Patent on Recombinant DNA Technology

### Learning of the Invention

#### Reimers

The news director at Stanford, Bob Beyers, had a practice, and I don't think it's done anymore. If he saw something that would be of interest relating to the educational world--he compiled something called the "Educational Digest" that he circulated at Stanford once a month or so--he would photocopy these articles he saw in newspapers and magazines and send them around. But if he found something specifically of interest for technology licensing, he would immediately get that off to us. In this case, it was an article from the *New York Times*,<sup>3</sup> not too extensive, about this work of Stan Cohen,<sup>4</sup> and that's the only name I really looked at at the time. It reported on the publication of Stan's work--this was in May of '74--and it looked interesting to me. Later that same day, I got a press release from Spyros Andreopoulos, who was head of the news service at the [Stanford University] Medical Center. It was the first tip I got from Bob that stimulated me to investigate it.

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### Negotiating with Stan Cohen and the University of California

#### Reimers

I called up Stan, with whom I had worked before, but not in this field. He had been in clinical pharmacology, and there he had developed some drug interaction technology, software based. So I had gotten to know Stan. I said, "Stan, this looks like it's interesting and important work." And he said, "Yes." He thanked me for that; he agreed that it was very important. "But, no patents. This is something that's going to go out broadly." I said, "Well, it certainly will, but if we apply for a patent on it, there's the concern about the safety of recombinant DNA research. Through a patent we might be able to get an exclusive license to a company to develop a recombinant insulin and so on. You can't get drugs developed today without some proprietary protection, because they require an investment of a couple of hundred million dollars for R & D. So through the mechanism of the license we would be able to do that sort of thing. We could require companies to follow safety guidelines also, through the mechanism of the license." Then I explained to him how patents worked. Stan finally agreed to cooperate and then added, "There's a co-inventor on this, Herb Boyer, and he will have to agree as well." I said, "Fine."

At UC, the technology is controlled by the UC Systemwide office. So I contacted Josephine Olpaka, who worked for Mark Owens, a lawyer who was handling the UC licensing office. They were overloaded with technology, but the program had never made any money (over expenses).

#### Hughes

What do you mean overloaded by technology?

#### Reimers

Overloaded with technology that they didn't move. They did not market; they'd wait for a company to come to them, instead of taking the very proactive way that we did it at Stanford. So this invention of Cohen and Boyer was just one more thing to do.

Herb agreed that we could go forward. That meant negotiating with UC, so I drafted an inter-institutional agreement. UC Systemwide did not want to take any risks, so they wouldn't cover any patent or marketing costs. Everything would be at Stanford's risk. I said that 15 percent off the top would go to Stanford for managing the patent. Then Stanford could recover its expenses, and then the balance would be divided fifty-fifty. But if nothing ever came in in royalties, Stanford would be out whatever they had spent on it. This was the essence of the inter-institutional agreement that was signed. Of course, later on the licensing proved to be successful. UC then thought that 15 percent was an over-recovery, and I told them, "You had your chance."

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### Commercial Potential

#### Hughes

Did the *New York Times* article spell out the applied possibilities of this technology?

#### Reimers

It talked about the potential. Stan and I disagree on this one point, by the way. My recollection was, Stan thought that commercial use was far out there in years. He now says he realized then it would be a shorter period. I explained that the patent runs seventeen years, and he thought the real big money wouldn't come until later. He's quite right in that. But, of course, we were able to get a fairly decent return before the patent expired [December 1997].

**Hughes**

He was saying that the patent would expire in seventeen years and there probably wouldn't be much profit in that period of time?

**Reimers**

Yes. But that's an area where we decided to agree to disagree.

**Hughes**

From the very start that was his attitude?

**Reimers**

No, later, when I was giving a talk on this, I had mentioned that he didn't think that there would be any significant commercial applications for many years. He says, no, he anticipated it would be earlier. It probably was my interpretation of what he said. He may have said that any significant money may not come until the patent expires. As it turned out, we had a difficult time in the [U.S.] Patent [and Trademark] Office, which in a sense, turned out to be advantageous for us, because it's seventeen years from issue.

**Hughes**

Well, let's go over it step by step. Did Beyers send you this article with the idea that this might be patentable research?

**Reimers**

Well, no. It was a piece of technology of a Stanford professor; Beyers would have no idea whether it was patentable or not. He was just keeping me informed. That publication, by the way, after I talked to Stan, led me back to a 1973 publication, November of 1973,<sup>5</sup> which had disclosed it before, but it didn't get any attention at that time.

The only reason Stan's publication got attention in May of '74 is that a reporter [Victor McElheny] from the *New York Times* was going to do an article on--I forget the topic--something from a Harvard or MIT professor. The scientist said that it really wasn't ready; he had to do some more science. And the reporter said, "Oh, gosh, I need to have an article." The scientist said, "Well, I think this is interesting work by Stan Cohen"--he may have said the others [authors]; I forget who was on the publication. My focus was on Stan Cohen and Annie Chang, who were at Stanford.

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**Hughes**

It was [Robert B.] Helling and Boyer on the UCSF side.

**Reimers**

That's right. Helling was on that. And that became a problem later, which was not in the publication.<sup>6</sup> The reporter then contacted Stan. So it's just by happenstance that that article was written. Otherwise, the research may have just lain fallow in the journal.

Before that time, the research results of people in biochemistry and genetics and such were fertile ground for Nobel Prizes, but not much for commercial application. In fact, when this whole industry [biotechnology] got going, they just did not have people in companies that had competence in the biological sciences. So this was quite a change. And there was a great demand for graduates in these fields at that time.

So I got UC signed up. Then I got the inventors signed up. Well, actually I only got Stan signed up, because UC signed up Herb. In the inter-institutional agreement, UC had to assure me that they had Herb signed up.

## Contacting Herbert W. Boyer

**Hughes**

After your conversation with Cohen, you had a conversation with Boyer, right?

**Reimers**

Yes.

**Hughes**

Can you remember the substance of that conversation?

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**Reimers**

No, I'm fuzzy about it. It could have been through the UC [patent] administrator.

**Hughes**

Well, you know how it might have happened. I went through the documents at OTL, and I noticed there were notes,<sup>7</sup> not by you. [interruption; Hughes hands copy of notes to Reimers.] Mr. Reimers is looking at notes taken by a Bill Carpenter, who was a student?

**Reimers**

A business school student. I made it a practice to have business school students work with me every summer, and then part-time during the rest of the year. It was the summer between their first and second year of business school. And Bill was excellent.

**Hughes**

So he obviously had had a conversation with Boyer, which doesn't mean that you also didn't.

**Reimers**

It probably is the case. It probably was Bill. And good for Bill. I'm glad the note was in the file. But I knew that Boyer was ready to go forward. And that's probably why I'm fuzzy about that contact.

**Hughes**

Was Boyer immediately ready? He didn't have Stan's hesitations?

**Reimers**

No, not that I recall, or even through Bill. Boyer was very straightforward, and we went on. I don't think at that time he had been contacted by [Robert] Swanson.<sup>8</sup> I don't think it was until we started to get some publicity about the commercial potential of recombinant DNA.

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## Negotiating the Institutional Patent Agreement

**Reimers**

So we got the inter-institutional agreement with UC worked out. The research at Stanford had been sponsored by, I think, NIH [National Institutes of Health], and at UC by NSF [National Science Foundation] and the American Cancer Society. The American Cancer Society had never released rights on an invention before. So I contacted them and explained the situation. I said that what I'd like to do is have it managed under our institutional patent agreement with NIH. And I explained the patent system and how the net returns would go back into research. They eventually agreed.

**Hughes**

Did every educational institution that was receiving money from NIH have an agreement with NIH?

**Reimers**

No, you had to negotiate an "institutional patent agreement." In 1980, I was involved with lobbying the Bayh-Dole bill through Congress. That then gave universities automatic rights, first option to rights, in all inventions created with government money. But at the time of the Cohen-Boyer invention, we had to negotiate specific agreements with each agency. So I had an institutional patent agreement with NSF as well as NIH. But the invention fell more in the NIH camp. NSF said we still had the obligations to them, and we would need to report to them and so on, but they would agree that NIH could take the lead. So that's how it ended up.

By the time that last agreement was inked and the patent application filed, it was one week before the patent bar. It was late, very late. I had engaged Bert [Bertram I.] Rowland. He was one of the few patent attorneys that had knowledge in this field at that time.

**Hughes**

You mean in biological science?

**Reimers**

Yes. He had gotten his Ph.D. at the University of Washington, very knowledgeable in that.

**Hughes**

In biology?

**Reimers**

Yes. What we now call biotech, biochemistry. It was filed one week before the absolute patent bar. Because we filed after the publication by Cohen, Boyer, et al., the only patent rights we could seek were U.S. rights, and that application had to be filed by November of 1974.<sup>9</sup> So I hadn't given Rowland too much time. There were a lot of tense times with the safety issues and so on.

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**First Description and Anonymous Review of the Invention****Hughes**

The first description I saw of the very preliminary stages of a patent application, I suppose, was written on October 18, 1974.<sup>10</sup> It was called Plasmid Gene Transplantation Technique. Of course, you've since changed the nomenclature.

**Reimers**

Well, we made it a little more descriptive.

**Hughes**

[hands document to Reimers] Did you write that?

**Reimers**

I doubt it.

**Hughes**

It's by Bill Carpenter, presumably. At least he's on the memo.

**Reimers**

Oh, it's his handwriting.<sup>11</sup> Yes, that was Bill.

**Hughes**

Apparently you sent out this preliminary description.

**Reimers**

We sent that to Cohen and Boyer, asking for feedback.

**Hughes**

Yes, but you must have also sent it to somebody else because there was an anonymous review.<sup>12</sup> May I read the first paragraph?

**Reimers**

Sure.

**Hughes**

It says, "In response to your request for the evaluation of the patent application entitled 'Process and Composition for Biologically Functional DNA Chimeras' by Cohen and Boyer, I would like to make the following comments."

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The first paragraph reads:

To begin with, this technological development very clearly has immediate applications and probably represents one of the most outstanding new developments in molecular biology in recent years. It is a far-reaching development and has extremely high potential with respect to its commercial application. If the patent is successful there is little doubt that it represents a potential source of considerable amount of royalties for the Universities involved. With respect to the feasibility of the project, it clearly is based on sound biological principles and does, indeed, represent a novel development.

**Reimers**

Do I recall who did that?

**Hughes**

Yes, do you?

**Reimers**

[long silence]

### Hughes

Was it common procedure to ask for a review?

### Reimers

My sense was that I had something that was potentially very important, and I wanted to get feedback on it.

### Hughes

You don't know who the anonymous reviewer might have been. It's somebody, obviously, who could appreciate the science.

### Reimers

Yes, here he talks about the early work. I'm trying to think who I was close to at that time, that might have done it. I needed to get someone fairly objective, I felt; it was probably not a Stanford or UCSF person.

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## Paul Berg's Reaction

### Reimers

Some emotions were involved with all of this. I remember Paul Berg wanted to meet with me, and he was quite upset that I had filed on this case, very upset.<sup>13</sup> Then he noted the work that he and his student--Janet Mertz--had done earlier. I said, "Everyone stands on the shoulders of the scientists that have worked before. Had you disclosed your earlier work to me, and it was something that could be applied..." In other words, you can't patent just an idea; you have to have a teaching in the patent, so you can make that insulin product, and so on.

So if Berg's research was that far along, and he had disclosed it, then I certainly would have gone for it by applying for a patent. As it turns out, he was probably close to doing that, but he was working then with--

### Hughes

He was working with SV40 [a simian virus].

### Reimers

SV40, yes. And SV40 had some safety concerns. So, he held back. You'd have to talk to other scientists as to whether he could have done what Cohen and Boyer successfully did, or not. But he didn't. And so Stan and Herb were clearly first. Stan was not in the inner circle at Stanford, or perhaps elsewhere, because he had been, if you recall, in clinical pharmacology. He may not have been one of those they would have liked to have had do this. You'd have to talk them;<sup>14</sup> maybe he was an interloper in the field, or whatever. There was not universal joy in the biochemistry establishment about what I was doing.

### Hughes

Why were you convinced that this invention could be something big?

### Reimers

I wasn't convinced. I didn't know that much about it. Because a great excitement developed regarding this area, I maintained from the beginning that this work of Cohen and Boyer would underlie the whole field of biotechnology. And I repeated it and repeated it. When I first went licensing, a lot of the companies, the business people, didn't really understand the technology. They had just been reading about its potential. Now, that was true of some of the companies, not all of them. So we had to go through a tutorial as well.

By then I had a couple of other business school students. I saw Ken Imatani's name in your documents. Then I hired Andy Barnes, and Andy was just super helpful. He was just graduating from the business school, and I felt I needed somebody full-time to help me on this. And so he agreed to work full-time. So Andy and I developed all these documents and visuals that explained the patent and the four royalty elements.

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## Explaining the Patenting Process

### Hughes

Let's wait a bit on that. Let me just read the last paragraph in this review, because it brings out some of the problems that you're going to confront as you apply for the patent.

In summary, it is my view that this is a somewhat ill-conceived patent application that disregards (albeit unintentionally) the contributions of other scientists and is very basic in its concepts and applications. While one can argue that the University should

attempt to benefit from this scientific achievement, I am concerned that given the fundamental nature of the work and the number of scientists involved, either directly or indirectly, that this patent will not reflect favorably on the public service ideals of the University.

### Reimers

I mentioned that biochemistry is the fertile ground for Nobel Prizes and that sort of thing. Few biological scientists had been involved with the commercial side. They didn't understand the role of patents, such as the patent is an ultimate publication. A patent provides much more information than the typical publication. You have to, or the patent will be invalid. You have to teach how to go forward. And it does not in any way restrict publication. I had to work almost one on one with each scientist to explain the system to them.

It's not like an academic publication. Yes, if you need to explain the science, the teaching part of the application, you would refer to work by others. But if there wasn't a teaching element, you might not refer to other scientists' work. But in a [scientific] publication, you have got to refer to those who came before. The perception was that the patent was restrictive. They didn't understand the basic principle: patents do not inhibit research, because that's a public policy issue. The right to patent goes back to the [U.S.] Constitution.

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### Hughes

What became an issue, and what to this day is an issue, is that in certain instances scientists do hold up publications until they can get patents filed.

### Reimers

Oh, it's terrible, yes. In my career at Stanford, MIT, UC Berkeley, and UCSF, I have never delayed publication--not for a year, not for a month, not for a week, not for a day, not for an hour, not for a minute, not even a second. When people said, "Well, if you haven't had enough time to evaluate my technology, to decide to file a patent on it, I can hold up publication," I would tell them, "No."

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— [Begin Tape 1, Side B] —

## Royalty Distribution ##

### Reimers

I had to be a little cynical about Art [Arthur Kornberg] and Paul [Berg] because they got involved with DNAX [1980], and DNAX was sold to Schering-Plough not long after it was founded.<sup>15</sup> The key asset that [Alejandro] Zaffaroni had in that sale was the tie-in with Paul and Art and perhaps a few others. So I was just estimating backwards of what financial piece they got out of that, and it was much more than Stan had gotten up to that point. In fact, Stan had initially waived his right to personal royalties, because everybody was all over him; he didn't want to be tarred with that brush. I think, he didn't even give his royalties to Stanford; they went to his alma mater, which was the University of Pennsylvania, I believe.

### Hughes

He graduated from the University of Pennsylvania.

### Reimers

Yes, so he gave them to Pennsylvania. However, later he decided, perhaps based on what others were doing, that he would take the money himself.

### Hughes

When was that?

### Reimers

It should be in the file. Let's see, the first intern came in when we did our first license. Was that 1980?

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### Hughes

The process patent issued in 1980.<sup>16</sup> You certainly began actively soliciting licenses in 1981, and that was when Andy Barnes was very active.<sup>17</sup>

### Reimers

[musing] So it was in the fall of that year, December 15, 1981, when all that money came in. And then that year's income was distributed the fall of the next year, the fiscal year that ran through August 31, 1982. It probably would have been '83 or '84 that Stan decided to accept personal royalties. I said, "I'm going to tell people, because I

publicly said that you were waiving your royalties. And if anybody said that they understood that you waived royalties, I'm going to explain that you did, but now you don't, and then refer them to you." He pointed out he could still be donating them. I said, "That's fine. You deal with that."

### Hughes

Does Boyer receive personal royalties?

### Reimers

No, I am told he turned them over to UCSF, to the Department of Biochemistry.<sup>18</sup> I haven't seen the documents; you'd have to talk to Herb. He made a ton of money through Genentech.

It's interesting. I don't think to this day, Stanford has received patent disclosures from Paul or Art. But from quite a few others.

## Controversy over Patenting in Biology

### Reimers

I think it's important for scientists, if they can't aid the process by which results of their research are delivered in a form the public can use, they should at least not inhibit it. And I don't think people are inhibiting the process, but it's better if they aid the process. If Paul or anybody has come up with something significant, a drug won't be developed unless we can get a patent on it.

### Hughes

In biology, there wasn't that long tradition of patenting that there had been in the physical sciences.

### Reimers

Yes, it's coming out more and more.

### Hughes

You were probably on the first wave in biology.

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### Reimers

Yes.

### Hughes

What complicated these issues and made people even more skittish was the fact that the recombinant DNA controversy was almost synchronous with the patenting attempts. And who was most prominent at Asilomar? Paul Berg.

### Reimers

Exactly. There was a conference at MIT on recombinant DNA, and Stan--he may have given a talk earlier--was leaning against the wall in the back of the auditorium.

### Hughes

Oh, the Miles symposium [June 8-10, 1976].

### Reimers

And somebody said, "What about the patent applications? We understand, there are patents. Stan Cohen may know something about that." Stan told me, "That was a long walk down the aisle [to the podium]." But he says all the way along he was trying to remember what I had said about the basics of the patent system, and so on. And when he got up there, he essentially diffused the situation and explained it. At that time he was probably talking about the fact that he was not taking any personal royalties; any monies received went back into research.<sup>19</sup>

### Hughes

Yes, but I think he also was trying to explain that patenting would not affect academic research.

### Reimers

Right. By the way, we had some disagreements as we went along, Stan and I. It was not all peaches and cream. As a matter of fact, Sally Hines was in my office. There was essentially just me, Sally, John Poitras, and the [business school] students. She or another person there said that, gosh, they were worried about me, because Stan was raising his voice.

### Hughes

Do you remember what the issues were?

**Reimers**

No, I honestly don't. But some of it was, he didn't quite understand the situation. What we do is a complex mix of business, technology, and law.

Stan was very interested in what was going on, but maintained that he wasn't. But I put a note in the file every single time I talked with him on the phone. You probably saw them when you went through the files. Stan is a wonderful guy; he's very tenacious.

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**The Licensing Plan****Claims to Inventorship****Hughes**

Well, I want to show you a July '76 licensing plan<sup>20</sup> and see if it brings back any memories. This is the first one that I saw.

**Reimers**

Yes.

**Hughes**

Was there a debate about the inventors being solely Cohen and Boyer?

**Reimers**

Yes, there certainly was. And you can get that from the patent file history; it's public. The University of Michigan was trying to assert that Helling was a co-inventor, because he was on the publication. Annie [Chang] wasn't a co-inventor. But based on patent law, it was Herb and Stan. Stan had the plasmid, and Herb had the enzyme. And they agreed to collaborate.

**Hughes**

How did you discount Annie?

**Reimers**

The patent attorney makes the decision. It was a non-issue with Annie: she was carrying out the experiment, but she wasn't the inventor. But the patent attorney determines that; I don't determine that. At that time, patent law was even more stringent than today about who is the inventor, that you don't put on people who aren't inventors, and you don't leave off people who are inventors.

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**Hughes**

The Helling problem came later. What I'm asking is, at the time of this licensing plan, were you discussing who should be the inventors?

**Reimers**

Oh, no. The inventors were determined in 1974, and this was '76. During the patent prosecution process, after we had filed, then there was a call from the University of Michigan. In some ways, I didn't care a lot about that, because Boyer's royalties would come out of the UC half. Royalties were divided equally between the universities, and then we would divvy ours out based on our policy. UC would divvy theirs out based on their policy. So, Helling, in that sense, wasn't a concern to Stanford, except for the fact, from the patent point of view, we had to have the correct inventors. So that meant it needed to be dealt with publicly before the patent office, which it was.

By the way, a sore point for Boyer is somewhat understandable. Stanford took 15 percent for managing the case, and at UC, the standard practice was 15 percent off the top for managing the case, and then you distributed. Well, UC took another 15 percent. All they had to do was cash the checks from Stanford, but they took another 15 percent. So if you want to get some sharp reaction, talk to Herb about that. [laughter]

**Hughes**

They took 15 percent off the 50 percent that went to UC?

**Reimers**

Yes.

**Hughes**

Yes, that makes a difference, doesn't it?

**Reimers**

Big difference. I mean, you're talking big money. I got a chance to talk to Herb about that. I didn't know that UC took the 15 percent until I saw Herb last year, and he mentioned that to me.

**Hughes**

How was the Helling claim handled?

**Reimers**

It was through communication with the University of Michigan, and through the patent office by Bert Rowland. Bert Rowland took the lead for us in that. He handled the inventor question. And as I say, it was to the benefit of UC, well, not the benefit of UC. In a way, it was only to the benefit of Herb Boyer, as the "inventor's share" at UC would be divided among two people rather than one. But the key thing was, we wanted to get the inventorship right, and there was no negative feeling toward Helling or the University of Michigan. Helling's claim was probably sort of annoying; it was disturbing things. But it got resolved.

**Hughes**

Resolved on the grounds that the concept had come from Boyer and Cohen, and Helling was an implementor, rather than an inventor?

**Reimers**

Yes, Cohen and Boyer described under testimony just exactly what he did, and it was determined he didn't contribute to the invention. The thing about this business, somebody can do all the work and not be the inventor if they're simply the hands of the experiment.

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**Hughes**

So it's the idea that is important.

**Reimers**

Yes. And publication co-authors may not appreciate that, because in academic publications you put down everybody who was involved, and of course Helling's name was there on the paper.<sup>21</sup> He had been on sabbatical from the University of Michigan during that time.

**Hughes**

I pulled you away from the July '76 licensing plan. Is there anything you care to say about it?

**Reimers**

Oh, I just felt I needed to write something up. And maybe to explain where to go forward.

**Ken Imatani****Hughes**

I saw some documents by Ken Imatani, who I gather was another student from the business school?

**Reimers**

Yes. I still see Ken. I play golf with Ken every now and then. I stay in touch with my students.

**Hughes**

He did what looked like a market analysis.<sup>22</sup> Was that the basis for your discussion of the market here?

**Reimers**

Well, there was a lot of stuff being written at the time. Different students had different backgrounds. Ken was more analytical. Bill was more of a marketing type. Oh, here's the one from Ken Imatani. Okay, he had a discussion with Herb Boyer.<sup>23</sup> I asked him to talk with him about what further development work was going on, because that would be important to me in this. Herb at this time said that he wanted to get some funds to support organic chemists to synthesize [DNA] molecules. At this time, he probably had not been contacted by Swanson, is my guess.

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**Hughes**

No, he hadn't.

**Reimers**

Ken and articles in the paper and such led to the licensing plan.

**Rejecting Genentech's Request for an Exclusive License****Hughes**

Genentech was founded early in 1976; it was April when the incorporation papers were signed. Also by that time, actually somewhat sooner, Cohen had become a scientific advisor to Cetus. Did these commercial ties present any problems in pursuing the patent issue?

**Reimers**

No, not for me; that was totally separate.

**Hughes**

Well, in the perception of those on the outside, would those ties have been perceived as a conflict of interest? For example, one of the companies that became most interested in this technology early on was Genentech.

**Reimers**

Yes, I'll tell you about my first meeting with them.

**Hughes**

Yes, I'd like to hear.

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**Reimers**

I had absolutely no problem with that. Typically, we licensed exclusively, because most university technology is undeveloped. And to encourage investment to develop a product, you need to give an exclusive license. That's very typical of university licensing. But when you've got a basic tool, such as this, you want it to get out broadly and nonexclusively. I did early on think that maybe we could give a field-of-use exclusive. But as I learned more about this recombinant DNA technology, I felt that this was something that we'd want to get out to everybody, as broadly as possible. I wanted to get it established early on as sort of the fundamental patent building block of the whole field.

So I was contacted by Swanson, and met with him and Tom Kiley. Tom Kiley was an attorney with Lyon and Lyon in Los Angeles, and it was he whom Bob was working with to develop the company. Bob was an associate with the Kleiner & Perkins venture capital firm at the time. When I was in San Francisco for the meeting, I talked briefly with either Gene [Kleiner] or Tom [Perkins], and then there was this very young-looking fellow, Swanson, and Tom Kiley. They wanted an exclusive license for all polypeptides. Tom gives very dramatic presentations, and he'd be ferocious in the courtroom, as a lawyer. But I knew where I stood, and there was no doubt in my mind of the appropriate response. I just smiled and said, "No." I don't believe they were optimistic Stanford would agree, but it was worth a try.

There was a meeting called "Alliance" put on by Recombinant here in San Francisco a couple of weeks ago at the Ritz Carlton, and there was some reminiscing about the early beginnings of the biotechnology industry. George Rathmann, Bob Swanson, and Bill Rutter were on a panel. I think it says so here in the program. I was on a subsequent panel; my presentation didn't have to do with reminiscing, but I did a little because there was interest in the early days. I had to mention a few things that I thought the audience might find of interest. One was an anecdote involving a meeting with George Rathmann. The other was with respect to Swanson, telling about that meeting where they asked about an exclusive license to polypeptides. I talked later with Tom Kiley, who was at the meeting as well, and Bob, and they also reminisced about that meeting with a slightly different spin. But they were laughing. They realized my attitude was, "Nice try guys." And they knew that. It was friendly.

**Hughes**

Were they at that stage worried about the future of their baby company? To not get an exclusive license jeopardized their future, did it not? Or, were they enough ahead of the game?

**Reimers**

Well, what they've gained from that meeting was that the patent would be licensed at a low royalty, because this license was going to underlie commercial activity in the biotechnology industry.

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**Worries about Patent Coverage****Reimers**

By the way, in the setting of the royalty, I got one letter from an alumnus: "You've got a patent; you can dominate everything here. Why are you charging such a low royalty? You know Stanford could use the money. Charge a higher royalty."

I had to smile because he obviously didn't understand the full situation. For one thing, it was a bit flaky, whether we could make this or not, whether we had adequate coverage in the patent specification for prokaryotes, hosts, and eukaryotes, and whether we could get broad patent claims. And also there was another factor: we only had U.S. rights. As a patent gives the right to make, use, and sell, somebody possibly could use our process overseas, and then sell the non-infringing end product back in the United States.

We then dealt with that issue in part through the International Trade Commission [ITC] and part through the royalty structure. The ITC (a U.S. government commission) is concerned with a level playing field and fairness in cross-border trade. If, to avoid a U.S. process patent, a company sets up a manufacturing operation outside the U.S., the ITC can stop importation of the resulting products to the U.S. We obtained, and made public, a legal opinion, we could use the ITC mechanism. The issue became moot when, after the Supreme Court's five-to-four decision on "patenting of life," [1980] we obtained patent claims to products.

In devising the licensing program, a concern was that the genetic engineering steps of cutting and splicing DNA, and then inserting the resulting recombinant DNA in a microorganism host, whether prokaryotic or eukaryotic, was as far as our patents might reach. After the insertion step, then the modified organism--the transformant--expresses the high value protein desired. But it is essentially nature that is carrying it forward after the insertion step.

So it could be argued that the defensible patent coverage--I can talk about this now since the patent expires on December 2 [1997]--ends with the transformant. In other words, would I be able to enforce the patent on the end product of the expressed protein or just at the stage of the transformant?

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And then I had to realize some people might make some dumb economic moves, too. For example, a scientist might sell a transformant for small dollars to a company. And then I might not get the company to license the technology because of no enforceable patent coverage for the end product, the proteins that were being expressed by the transformant. The royalty was established at 10 percent at the level of the transformant. It was a factor of 20 from the transformant 10 percent to the end protein product royalty of 1/2 percent.

After we got the first group of licensees--you will see if you talk with Floyd Grolle--that there have been a number of changes in the royalty rate of subsequent licensees, all up. In fact, I don't know what it is now--it may be 2 percent at the end product level rather than 1/2 percent. But most companies that have become licensees recently are not worried about the earned royalty rate. They just don't want to be inhibited from practicing the technology; their sales of end product will be long after the patents expire.

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## Cohen's Involvement

### Hughes

Cohen initially said that he didn't want to be involved in the patenting process.

### Reimers

Is that from his notes?

### Hughes

I got that from notes about a conversation with Stan.<sup>24</sup>

### Reimers

Stan said he wanted to be excluded from licensing matters; he didn't want to be involved. In fact, as I mentioned earlier, he had little things to say all the time.

### Hughes

Also, he reversed himself. In June of 1976, he wrote to you saying that he wished to reverse his original request to remain uninformed about Stanford's activities in the licensing arena.<sup>25</sup> And it followed from that Miles symposium. Both you and Robert Rosenzweig responded.<sup>26</sup>

### Reimers

It's my normal practice to keep inventors fully informed of our licensing.

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### Hughes

Robert Rosenzweig disagreed, saying it was better for Cohen to be detached from Stanford decisions.

**Reimers**

I don't think Rosensweig really understood the whole complexity of the business, but I would agree with his decision.

**Hughes**

Also, don't you think he was looking at it--

**Reimers**

He was looking at it from a PR [public relations] standpoint. That was his role. He is a very savvy individual.

**The Biohazards Controversy****Hughes**

Also remember what these high profile people are dealing with.

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**Reimers**

The whole safety issue. Oh, I can tell you about this safety issue, which we went through for a time with NIH. Remember, I mentioned I was going to put in the license that it was mandatory for industry licensees to follow the NIH guidelines for recombinant DNA research. So I put in a requirement that the industry licensees follow the safety guidelines and submit evidence that they were doing this to the NIH--or HEW, the Department of Health, Education, and Welfare. The rights came from HEW, which is now HHS [Department of Health and Human Services]. NIH didn't want to be involved as an enforcing agency, even though they had gotten some PR concerning safety guidelines for industry. So we modified the license safety clause to satisfy NIH.

Academics had to follow safety procedures--P1, P2, P3 levels of physical containment, and levels of biological containment, such as an enfeebled *E. coli* host. But industry, because it wasn't receiving government funding, didn't at the time need to follow safety guidelines for rDNA research. So while I had trumpeted the fact that through the license we could require compliance with the guidelines, NIH didn't want to be a regulatory agency. So if you look at the license, you'll see that it reads that industry will make efforts to follow the safety guidelines, or something like that.

**National Institutes of Health****Hughes**

Right. In the summer of '76, you met with people at NIH. In fact, you wrote in July of '76, "The recombinant DNA patent issue is considered 'hyper-important' at NIH, with concerns about the media, the Congress, and the public."<sup>27</sup>

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— [Begin Tape 2, Side A] ## —

**Reimers**

I have a lot of old files in the basement that I thought I should keep. When I came to Stanford, I was starting the licensing program, and then I went back into the old files that I could find about the klystron patent. Other patents had been filed by Stanford in the past, but nothing had been done with them. I shuffled through those, and I found some of historical interest.

I took maybe half a dozen patents, max, down to where I was on the first floor of Encina Hall, and then Encina Hall was burned during the Vietnam conflict period. In the top part of Encina Hall were all the administrative records, including all the patent records, all of which were burned. So the only ones that were left were the half dozen I had, which are pretty; they have the purple ribbons of old patents.

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**Honoring Cohen and Boyer****Reimers**

That reminds me: I invited Julie [Julius] Krevans, who was chancellor at UCSF, and Don Kennedy, president of Stanford--neither institution had recognized Herb and Stan. So I arranged with a faculty spouse, who was a good painter, to have two paintings made and framed of an artist's representations of DNA. One I didn't like so well, so she made a third one for nothing, so there were three paintings. And then I had the process patent and the product patent framed. Then Herb and Stan signed an agreement: if we needed those in litigation, they'd have to give them back. So Cohen and Boyer were given two framed paintings. Then the extra painting, which I wish I had kept, I gave to Bert Rowland, our patent attorney. So I've got nothing, except for my memories.

No, actually we did get this award, which probably doesn't belong to me but to Stanford. That award is why I wrote the paper.<sup>28</sup>

### Hughes

Please read the citation for the record.

### Reimers

Oh, it says, "The seal of the American Chemical Society." And it's a metal plate on a walnut plaque. "Stanford University, University of California in recognition of their innovative cooperative licensing of the Boyer and Cohen patent, United States patent number 4,237,224." And in smaller letters: "ACS Division of Chemistry and the Law. ACS Committee on Patents and Related Matters, 1986." The paper was written for the award, because they wanted a paper along with that. Hughes; "Tiger by the Tail."

### Reimers

Yes; the journal editor gave it that title.

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## More on the Licensing Plan

### Criticism

#### Hughes

Getting back to the controversy that surrounded the licensing activities: At the time, was Stanford viewed as having a conflict of interest in pursuing the patent and at the same time being the major locus for discussing safety issues?

#### Reimers

Now, that was one of the things that Paul talked to me about. Here we are filing a patent, and here they are taking the lead in the safety issues, and some could perceive that we at Stanford were just trying to cement our proprietary position, while others were required to hold back in research using recombinant DNA technology. And so, partly as a result of that, Stanford could have been viewed as having a conflict of interest.

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Many articles began appearing in the paper about whether doing rDNA research is the right thing to do. But also articles about commercialization: the commercial world is going to get in there, and they are *really* going to do bad things. So that's when I recommended, and it was agreed, that we essentially go back to the NIH, which was the government entity with which we were working on this, and give them the opportunity to deal with the patent rather than Stanford, if Stanford's actions were not considered in the public interest. And Rosenzweig wrote that letter; it's in Watson's book.<sup>29</sup>

After the Rosenzweig letter was received at HEW, I talked with Norm Latker [patent counsel for HEW]. He told me they were uptight on matters about rDNA patents. At an HEW meeting on the topic, he walked into, as he put it, "a den of scientists without a patent understanding." He had to educate them about the patent system and its role in commercial development. HEW considered a number of alternatives, including abandoning the patent application.

Then in the Senate hearings in 1977 on recombinant DNA research, Teddy Kennedy got involved. By then, HEW had the education on the role of patents and decided it would not be a good idea to take over the patent. What message would that send out to other HEW grantees who sought to develop the technology so that the public could use it, if the government would march in to take back any patent with significant commercial potential?

I listed in the article<sup>30</sup> what Norm told me about the different options that HEW had been considering: dedicate the patent to the public, don't allow it to go further, take it back, take it back and NIH will restrict this and that. They had about six different considerations. The final determination was, let Stanford go for it.

#### Hughes

Do you know why they eventually decided on that option?

#### Reimers

Well, I would suspect it was because of Norm's activities explaining the patent system, similar to what happened at Stanford in many respects. Norm was a wonderful guy. He's very much an advocate, in intensity, like Ralph Nader. He's very much an advocate for not simply filing patents, but having the technology behind that benefit the public somehow by being developed. So he was very much a staunch supporter of universities that would file patents and get technology developed. The university community and the public owe a lot to Norm.

#### Hughes

Well, another criticism that arose in the late 1970s was that recombinant DNA technology had already been widely adopted. In fact, companies were founded on that basis.

#### Reimers

Sure, before our patent issued [1980].

### Hughes

Yes. Was that a stumbling block?

### Reimers

Well, no. I typically like to be at the front end of technology transfer. That is, we approach companies and propose we work together in developing this technology. We'll file the patent, we'll exercise the right to exclude others, and we'll develop it together. Well, when you do nonexclusive licensing, in a way you're just applying a tax. But I had no shyness about that here.

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## Opening Patent Files to Public Scrutiny

### Reimers

I do not like "submarine patents," as they are called. A submarine patentee files a patent but does nothing to develop the technology of the patent. The submarine patentee lies in wait for companies to invest their resources at risk in developing commercial applications. If a company achieves market success, the submarine patent owner begins legal action against that company. That is not technology transfer. We were not lying in wait, but were totally open about our plans to license. In fact, we did something that nobody in the Patent Office can remember applicants doing before, and that was that we opened up the patent prosecution process to public scrutiny.

To enforce this patent, I engaged the Finnegan, Henderson, Farabow and Garrett law firm in Washington, D.C., specifically, Don Dunner, Charlie Lipsey, and Susan Griffen. We called them Bruno, Boris, and Brunhilde. These names were actually suggested by Charlie, when we said a key purpose of engaging them was to be ferocious enforcers for us should the need arise. We were preparing for a defense of the patent, even though we had no challenges. Also, I wanted to line up the best litigation attorneys that I could, because later on if somebody sued us, then we'd have to scramble for litigators. And the best law firm might be beholden to others and not be available. In fact, we had to get permission from SmithKline, for whom Don Dunner was a counsel, to let us employ the Finnegan firm for this purpose. I talked about that with Janice Williams, SmithKline's head patent counsel. She was very gracious to say that was okay, to tell Don Dunner that he could accept the assignment with us.

After the law firm's review of the file history, including the means by which we made the patent prosecution process open, Don Dunner said that we had probably the highest presumption of validity of patent he had ever worked with, because any company would have to justify why they didn't bring forward any competing art to the Patent Office. At the time, this was all open to public scrutiny. It was in the newspapers; everybody knew about it.

Al Halluin, who was with Exxon then--his strong interest in biotech was called Halluin's Hobby because Exxon was not in the biotech business--was hired by Cetus. Al was their patent counsel who did the well-known PCR [polymerase chain reaction] patent work at Cetus. Al Halluin is now with a patent law firm here in San Francisco. Jim Watson had a conference on "Patenting Life" back at Cold Spring Harbor. Al was there, and he listened to me, Bert [Rowland], and some others speak. And then he wrote a post-conference paper about how our patent application wasn't worth anything because of this, this, and this.

Well, the beauty of it from my standpoint was we could deal with it there in the Patent Office as we presented his paper to the patent examiner. If he had kept quiet about these things, then if somebody was taking action against our patent in court, it could somehow be alleged that we were withholding that information from the Patent Office, and it could have narrowed the patent. So we were able to deal with it in a unemotional setting, if you will, an objective setting rather than before a jury. And I know that some patent attorneys, or companies, were very upset with Al for having published his article. If he hadn't, then they could have used the citations in Al's article as a means to invalidate any resulting patent.

## Setting a Low Licensing Fee

### Reimers

By the way, we set up a licensing plan, and with the modest royalty rates, there was no way biotech firms could not take a license. I talked to licensing officers at several companies in the course of promoting our licensing plan. They said if the royalties were any higher, they would have refused to take the license. We would have had to go through litigation to enforce them taking the license.

### Hughes

And I know you had set aside a fund to do just that.

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### Reimers

Yes.

### Hughes

Which you, in the end, did not have to tap?

#### Reimers

I tapped it to pay for the attorneys to prepare for litigation, but that was all we took from the fund.

### The International Trade Commission

#### Reimers

During this process, I went back to meet with the International Trade Commission [ITC], and Andy [Barnes] came back with me. The International Trade Commission is set up, among other things, for a situation where somebody would have a process patent, but only in the United States. Then somebody could make the product over in China, or Germany, or anywhere outside the U.S. And then they would ship the non-infringing product back into the United States, and they would not have infringed the U.S. patent, because they would have used the patented process in a country where the U.S. patent holder did not have a patent.

So the International Trade Commission was set up to deal with that sort of thing, and it's a very quick process. They had dealt with relatively minor technologies, and here we came along with their ability to exclude from import to the United States an entire industry. They got excited about it. Armed with their support, we went to another attorney with the Finnegan firm who had experience with the ITC; in fact, he had worked there. He and Don Dunner then wrote an opinion that we could use ITC law to exclude imports based on using the patented rDNA process outside the U.S. Given we only would have U.S. rights, no license was needed for transactions that occurred entirely outside the U.S.

Tom Kiley of Genentech told me later that Genentech followed us into Japan. This was during the licensing process when we had meetings with many companies. Tom said, "They had gotten the very clear message from you guys: it's either take a license or get your socks sued off." And those are his exact words.

#### Hughes

Then there was also opposition from people within the medical school.

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#### Reimers

Like Paul?

#### Hughes

Yes; I wondered if there were others. It didn't give specifics in this letter from [William F.] Massy to Rosenzweig in 1978.<sup>31</sup>

#### Reimers

Oh, I think Bill was referring to--

#### Hughes

To Berg.

#### Reimers

Stuff he had heard from me, yes.

### The Patent as a Potential Source of Income

#### Hughes

Did you use the argument that the patent was certainly a potential and, as it turned out, actual source of income for the medical school?

#### Reimers

The interesting thing was the way I originally set up the royalty structure at Stanford, which was approved after that pilot year, and we had used it through the pilot year of 1969-70. That formula was 15 percent of gross income deducted for managing the program, and then we'd subtract out-of-pocket expenses to arrive at net income. Then one-third to the inventors, one-third to their departments (like chemistry, physics, biochemistry, etc.), and then one-third to the university, not the school.

#### Hughes

So the medical school didn't benefit directly.

#### Reimers

No, not at the beginning. The university was the one that invested the money for filing the patent, and so on. The university quickly began to make money. When that money started rolling in, then the medical school got involved. They said, we're different than the School of Engineering or the School of Humanities and Sciences in that we're under a general fund ceiling. So it's really not appropriate that the university get that third, because our tub has to stand on its own bottom.

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So Don Kennedy agreed to allocating "the university's one-third" to the school of the inventor; he didn't consult with trustees or anybody else. I didn't have any real objection to it. It was fine with me. The further down you push the incentives, the greater positive results you're going to get. So now I had the deans excited. [laughter]

**Hughes**

Now, this is in regards to patents in general or to this one in specific?

**Reimers**

Don Kennedy changed it for all patents, with the complaint from the medical school about this patent, because they were under a general fund ceiling. Every university is worried about the potential for cost of their medical school consuming the rest of the university. So medical schools have to essentially run themselves separately. They get a limited amount of general funds.

**Hughes**

When was that?

**Reimers**

It was probably the year after our initial success in the licensing program.

**Hughes**

So about 1982?

**Reimers**

Yes, probably.

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**Royalty Distribution****Hughes**

You mentioned that the Department of Medicine was one of the three beneficiaries.

**Reimers**

There was a question of which department would get "the department's one-third." Stan was in the Department of Medicine, plus another. The Department of Medicine includes the Division of Clinical Pharmacology, where Stan resided. I forget, but there were initially two departments, and then Stan was sort of changing his departmental allegiance.

**Hughes**

The Department of Genetics was another one of his appointments.

**Reimers**

Yes. So it was Genetics and Medicine. But within Medicine, he was in Clinical Pharmacology.

**Hughes**

Clinical Pharmacology got the money, so that Medicine as a whole didn't have access to it?

**Reimers**

I don't recall specifics. But there was a bit of discussion on that, and I believe the original split was modified. The Department of Medicine is so huge. They are disproportionately large compared to other departments of the medical school. In fact, now that we're down at the molecular level, the old departmental designations really don't make a lot of sense anymore. They really ought to change the medical school departmental organization. The Department of Medicine, I think, should be broken into more reasonable department sizes. But that's another story.

**Hughes**

One of the sore points, which persists to this day, is that Biochemistry did not benefit from the patent.<sup>32</sup> Certain members of that faculty believe that the Cohen-Boyer technology was based substantially on their work, and ergo

they should be recipients of some of the royalties.

### Reimers

Well, they could have gone to the Dean of the School of Medicine and made their case. But you know, Paul and Arthur are wonderful people; they have gotten the Nobel Prize, and that's worth a hell of a lot more than money. Plus, they have done very well with DNAX.<sup>33</sup>

The big discoveries that made lots of money came later--like human growth hormone, insulin, hepatitis B, and so on. If our guys at Stanford were in that great position, they could have been researching and filing patent applications on those potential products and made much more money. The patent for hepatitis B vaccine makes more than the patent for recombinant DNA. And human growth hormone is up there too in royalties. Well, actually, the patent for hepatitis vaccine doesn't make more, but it makes close to it. And its income is going to continue on after expiration of the rDNA patents.

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### Hughes

Because the patent isn't about to expire?

### Reimers

Right. Of the University of California patents, hepatitis vaccine is the number one royalty producer; then number two is the check they get from Stanford every year [for royalties for the recombinant DNA patents], then number three is human growth hormone. UCSF has more income from its inventions than the combined total of UC Berkeley, UCLA, UC San Diego, UC Irvine, UC Davis, UC Riverside, UC Santa Cruz, and UC Santa Barbara.

### Hughes

And it's the smallest campus.

### Reimers

Yes.

### Hughes

How do you explain that?

### Reimers

For any licensing program to succeed in a big way, it has to have a medical school, because their patents can become big hits. And engineering; they can be the most creative people, and a lot of companies will come out of engineering, sure. But big bucks from patents tend to come in the medical field. And part of that is because of the regulatory process. If patents weren't strong in the medical field, because of the cost of getting a new drug to market, the field would be chaotic; it wouldn't go forward. It's too bad the Stanford Department of Biochemistry didn't get a share of royalties.

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## Threat of Regulatory Legislation

### Hughes

By 1977 and 1978, there was legislation pending to regulate recombinant DNA research at the federal level, and in some cases, at the state level as well. Were you taking into account this context?

### Reimers

Yes, definitely. There was nothing I could do until we started licensing. When you're going to license exclusively, you license on a patent application. But if you are trying to license non-exclusively, who's going to pay you before your patent issues? You have to wait until your patent issues. There was really nothing I could do about that, nor did I want to influence, nor could I influence that.

### Hughes

You mean what--

### Reimers

Was going on with safety, and so on. There emerged the physical containment, P1, P2, P3 type of facilities, and the biological containment--that's not the right term for it. For an example of biological containment, Roy Curtiss developed an enfeebled *E. coli* at the University of Alabama. By the way, Curtiss's strain of *E. coli* was never really used. I understand it was too enfeebled for useful experiments.

## U.S. Patent Office

### Hughes

In 1977, according to your article,<sup>34</sup> the patent examiner, whose name was Alvin Tanenholtz, told Bert Rowland that he would only consider a process patent. Can you give me the background?

### Reimers

Well, it didn't end up that way, of course. Getting a patent is a process of negotiation between the patent attorney and the examiner. Typically, when you send in a patent application, the Patent Office rejects it, and then it's a process of overcoming the rejection, and getting rejected again and overcoming that rejection, until a patent is awarded. It's rare that the examiner looks at a patent application and says, "Okay, I'm going to issue it to you." Patent examiners get rewarded based on disposals. A disposal is a rejection, an award, or other formal action taken on a patent application. The Patent Office has a huge load of work. So to spend hours and hours on a patent application, they only get one disposal.

So what an examiner tries to do is find a bunch of publications that seem to relate to the patent application. (They will provide more specifics; I'm being a little cynical.) The examiner will say, "In view of these publications, everything you've done is anticipated, so your application is rejected." Then they sort of define the universe. Then you as applicant go back and you say, "This cited publication is irrelevant because it relates to fish; this one doesn't apply for this reason," and so on. If a citation is relevant, then we deal with it. The exchanges with the patent examiner could have been part of my worry about whether we'd get product claims or not. We eventually did get product claims.

## The Chakrabarty U.S. Supreme Court Case

### Hughes

Because the Chakrabarty case was not settled until 1980, there was a debate about whether you could patent an organism.

### Reimers

Yes, a "life form"; that's absolutely true. There actually were two cases. One was Upjohn, and one was G.E. [General Electric]. Upjohn backed out so that there could be focus on the G.E. patent of [Ananda] Chakrabarty. He forced a mutation in bacteria--he didn't use the recombinant DNA process--and the bacteria then became very efficient in eating oil.

There was a cartoon at that time, which shows a microscopic view of organisms developed to eat oil. There was a picture of a slide, and then there were black things all over, but they were cars. [laughter]

*Newsweek* or *Time* or another magazine had an article which said, "Universities hold fall sale." And it showed a picture of a carnival barker holding out a cane and pointing to spirals of DNA stacked up behind him. People in the audience of this cartoon were shown clamoring for the DNA, and on the side of this crowd, people were walking away with DNA under their arms. [laughter]

The Supreme Court decided, five to four--that's pretty close--that genetically engineered organisms are handiworks of man, not of nature, and anything made by man is patentable.

### Reimers

The patent issued shortly after the Supreme Court announcement, and a lot of people thought that our patent issued because of the Supreme Court decision. But that was the process patent, and we were going to get that anyway. We earlier had divided our patent application into two, one covering process claims and the other product claims. We were still arguing about the product patent, and Tanenholtz was treading water until the Supreme Court made its decision. We dealt with arguments by the examiner about whether we should get both prokaryotic and eukaryotic organisms patented. We had very few words in the patent application to support getting eukaryotes, which are the higher organisms. We had "cell," [following spoken with pause between each word:] the --one--word "cell." And it ended up being enough for us to get the claim to the eukaryotes.

## The Patent Specification

### Hughes

The document is called a disclosure?

### Reimers

Specification. A patent has two primary sections. One is called the "specification," which teaches how to practice the patented technology. The other section covers "claims," which set the metes and bounds within which the patent can be enforced.

**Hughes**

You can't go back and modify a specification?

**Reimers**

No, you cannot change it. You can change the claims, but you cannot change your teachings. What you have to go do is file another patent. But you only get the priority benefit from the date you file the second application. U.S. laws provide the inventor is the one first to conceive the invention. If somebody has filed in the intervening period, you'll probably have some difficulty getting patent claims corresponding to the specification of your second patent application. In other countries, the inventor is the first to file, rather than first to invent (conceive). There are many other complexities in the patenting process.

**Hughes**

I can imagine how difficult it must have been in 1974 to anticipate how this process was going to develop. Wasn't there an element of luck? For example, that the specification included the word "cell?"

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**Reimers**

Sure.

**Hughes**

Was inclusion of the word "cell" deliberate? You wanted to make sure that the patent covered eukaryotes?

**Reimers**

Well, we placed a lot of faith in Bert Rowland. I think if Bert had had twenty-twenty hindsight, he would have asked Cohen and Boyer, "Is there a reason why this can't apply beyond bacteria (prokaryotes) to higher organisms, like yeast (which is a eukaryote)?" They would have told him, yes, the gene splicing technique does apply to any cell, to any DNA, because it doesn't matter. So, Bert could have asked the question. But "cell" was in there and that did it for us.

**Hughes**

Arthur Kornberg maintains that he, and I think he includes others in the Department of Biochemistry, didn't at the time see the applications of this technology.<sup>35</sup> It wasn't until later that they realized that they had a revolution in their midst, so to speak. How cognizant were Berg and Kornberg, in your estimation, say in the mid-seventies, of what actually could come from this technology?

**Reimers**

Well, we're talking about an industry that then didn't exist. And it's easy with twenty-twenty hindsight to say oh, it was obvious. But I don't think it was totally obvious. Visionaries, like Swanson (founder of Genentech)-- He was a very young man who saw the potential and contacted Boyer.<sup>36</sup>

**Patenting and Licensing Monoclonal Antibodies****Reimers**

There was another major discovery that came along not too long after recombinant DNA, and that was [Georges] Kohler and [Cesar] Milstein's discovery of hybridomas. Hybridomas produce identical antibodies, termed monoclonal antibodies. Prior to the Kohler-Milstein discovery, antibodies harvested from the blood of animals injected with an antigenic source were polyclonals, a mix of antibodies. And they blew it there in the UK as far as getting a basic patent on the hybridoma process. The British Technology Group blamed it on the university, and the university blamed it on the British Technology Group. And I don't know where the real truth lies.

But if you look at the first publications of Milstein and Kohler, you'll see two co-authors, Len [Leonard] Herzenberg and Vernon Oi of Stanford. Len was a professor and Vernon was, I believe, a Stanford graduate student with him. They brought that technology back to Stanford. And I'll wager we were the first ones to license monoclonal antibodies.

**Hughes**

Do you remember when that was?

**Reimers**

I would say it was probably '78 or so, but I'm not sure.

**Hughes**

So before the Cohen-Boyer patent issued.

**Reimers**

Yes. At UC, it's Boyer-Cohen. [laughter] I started calling it Cohen-Boyer.

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**Hughes**

Yes, I noticed it's usually that way.

**Reimers**

I thought that recombinant DNA would have tremendous commercial application. But I was just a mechanical engineer. That summer vacation--I had about a month that year--we were going up to Montana. I took along Watson's *Molecular Biology of the Gene* of 1974, whatever the current edition was, so that I'd have some understanding of what in the world this was all about.

In each new technology, it's a question of learning the terminology, so you can converse with people. Not that the invention a scientist is describing is always rocket science. I mean they could be, but you just need to understand what the scientists in the field are saying.

## Closing the Cohen-Boyer Patent File

**Hughes**

You mentioned earlier in the interview that you opened up the patent file to the public.

**Reimers**

And much later we closed it.

**Hughes**

Why did you close it?

**Reimers**

What did Stan say?

**Hughes**

I'm not sure that I even asked him.

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**Reimers**

The public reason I think I mentioned in the article. But what was going on then regarding the patent application was that every time there was an office action-- Remember, I call it an office action, but the word is rejection. And so every time there was an office action, or rejection if you will, it would make the papers, because people were very interested in this. And Stan didn't like the heat. Like they could see the Helling affair in there. This was grist for the writers. But I agreed to close it, because we had accomplished our purpose.

**Hughes**

There are always personalities involved, aren't there?

**Reimers**

Yes. Well, Stan or Herb may perhaps find some faults with what I did, but they've made millions. But it's possible, frankly, that their involvement could be a factor that is inhibiting them from getting the Nobel Prize. And that would be sad.

**Hughes**

The fact that they were involved with commercial--

**Reimers**

With a patent, yes. And when you think of who is on the Nobel Prize committee that decides this.

**Hughes**

Well, it seems to me, if it were going to happen, it would have been at the time of the Berg Nobel Prize in 1980.

**Reimers**

I was so glad when he got that. That's worth, in my mind, a lot more than having your name on a patent and millions in royalties. I was feeling bad before then, because Paul was a distinguished scientist, and he had been very upset with the patenting process and not being recognized. I had a discussion with him in his office where we

talked about Janet Mertz, and so on. He was obviously not happy about things at that time. Well, he got the Nobel Prize. That's great. And Art got it too.

Then I had to smile when DNAX was sold. I knew how much it was capitalized for, what Zaffaroni sold it for, and you could back in reasonably what they each made. They made a lot of money, even though the university didn't benefit financially. But the university has benefited tremendously from them in other ways.

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### John Morrow's Claim

#### Hughes

We mentioned Helling, but there was also a protest in 1980 from John Morrow, who didn't want to sign a disclaimer without first seeing the patent application.<sup>37</sup> He had worked on the *Xenopus* research. Is there a story to be told there?

#### Reimers

No. I do remember that. But it's sort of vague. I don't think it ever amounted to anything.

#### Hughes

Morrow had supplied the toad RNA.

#### Reimers

To Stan.

#### Hughes

To Stan, yes. When disclaimers were sent around, he refused to sign, and also Helling refused to sign.

#### Reimers

This was our patent attorney doing a thorough job. Because what happens is, when you're processing a patent through the Patent Office, and you've got sixteen authors on a publication that describes it, and there's only one or two inventors, then the Patent Office is going to say, "Well, look, are all those other people inventors, too?" So to anticipate that situation, you supply to the Patent Office disclaimers from co-authors. So disclaimers were sent to them, because Morrow must have been a co-author as well.

#### Hughes

Yes, he was, on the 1974 paper.<sup>38</sup>

#### Reimers

But the invention goes back to '73.

#### Hughes

The 1974 work used eukaryotic DNA. Was that not included in the 1980 process patent?

#### Reimers

Because we filed later in '74, we would have put in all the inventive steps that had preceded. We had a patent based largely on that '73 publication, but not necessarily everything that we'd claimed by the November 1974 filing date. The recombinant DNA success was in the summer of '73, and it was reported at a summer meeting. And most of the scientists there realized how important this was.

#### Hughes

Was there any fanfare when the process patent finally issued in December of 1980?

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#### Reimers

We may have publicized it.

#### Hughes

You'd been trying to get the patent issued for a long time. It was no big deal, as far as you were concerned, when it finally issued?

#### Reimers

It was a big deal. It was the Stanford-UC patent for the basic technique in biotechnology which issued. And that was in the newspaper. And, of course, *Science* and *Nature* were following this.

## Stanford's Announcement of the Licensing Program

### Hughes

Well, there was a Stanford news release in August 1981, and another in November.<sup>39</sup>

### Reimers

We began doing the licensing in '81.

### Hughes

I want to quote a statement, which was attributed to you, in the November 1981 release: "[T]here's no precedent for this sort of program, seeking to license all companies who are using what is essentially the basic tool needed in genetic engineering." Is it really true that in no field--computers, engineering, agriculture, or anything else--that there ever had been such an inclusive patent?

### Reimers

I doubt it. But I'd have to ask somebody in the history of science. No, because a discovery of commercial significance generally would be an invention of a company, and they would want to keep that for themselves, as long as they could get advantage from it.

### Hughes

And then the news release went on to quote Donald Kennedy: "[The licensing effort was designed to] assist the process of technology transfer by making sure lots of players get into the game. This increases the probability of valuable new applications for human science."

### Reimers

It's fine that Don said that, but whether we licensed it or not, commercialization of recombinant DNA was going forward. As I mentioned, a nonexclusive licensing program, at its heart, is really a tax. He's correct in that we were letting every player in on the game. But it's not an action that made the industry grow. I guess you could say it provided some order. It sort of was a base line, and the industry proceeded from that point. But from a legal point of view, or from what a patent means, or what the license means, it didn't make the industry grow. A lot of people don't fully understand all facets of technology licensing, because it is, as I mentioned earlier, a complex mix of business, technology, and law.

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### Hughes

You are saying that the growth of the biotech industry was not dependent upon this patent?

### Reimers

That's right. Well, you've got to turn that around; you mean the license.

### Hughes

Yes.

### Reimers

It was dependent on what was behind the patent, but it wasn't dependent on the license.

### Hughes

Because the technology would have happened regardless?

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### Reimers

Would have happened. We were just, in one sense, taxing them. But it's always nice to say "technology transfer."  
[laughter]

## Pajaro Dunes Conference on Technology Transfer, 1982

### Hughes

Kennedy had said in a news release a few months before that he thought scientists should consider calling an "Asilomar II" conference dealing with the "rush to proprietary control" of recombinant DNA research.<sup>40</sup> He was very concerned about the commercialization of basic research. In 1982, he was the main instigator of the Pajaro Dunes Conference. Do you remember that?

**Reimers**

Don didn't involve me in that. He had some naive perceptions, but this was something that Don got into.

**Hughes**

Into what?

**Reimers**

The whole industry-university thing and commercialization. He did not really discuss it with people who understood the complexities of it. I don't mean to make a big deal of it, but it was his thing. He has a good sense for what is newsworthy, and I don't mean to put that down. But he probably realized intuitively that it would be important for Stanford in particular, because it was making all this money on the license, to talk about commercialization issues. The companies they asked to the Pajaro Dunes conference were all big ones. They didn't get to the little ones, which were the key players--particularly if there was any discussion of potential conflict situations.

**Hughes**

Swanson was there, and Genentech was not very big. But you're right; there were representatives from big companies.<sup>41</sup>

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**Reimers**

And then they excluded the press. You ought to talk to Bob Beyers about that.

**Hughes**

From some accounts, there was really no tangible outcome. I mean, there wasn't a firm policy established regarding university interactions with industry.

**Reimers**

I don't want to say anything. It had some PR value, I think.

**Hughes**

Kennedy was representing a fairly widespread viewpoint at that point.

**Reimers**

Sure. I fought against the commercialization. Publish! Get it out there! I was sort of an evangelist: If you don't want to patent, don't. If you don't want to deal with industry, don't. If you do deal with industry, that will have absolutely no impact on your scientific career or interactions with other scientists unless you personally choose to alter your behavior.

**Reimers' Ill Ease about a Licensing Opportunity****Reimers**

In fact, I got very upset with a professor, who shall remain nameless. This could have been a very big invention, but it much later turned out it didn't quite work. He had this particular organism, let me just say that, and I was going to license its use. It wasn't something everybody would want a license to, but quite a few would. It was also going out nonexclusively, and so I was promoting it. Then I found that he was not sharing the organism with his scientific colleagues. And not only that, the word that I was getting back was that it was because of patent considerations. And that angered me, because there's no way that he should restrict sharing his research results with other scientists. The patent is another matter.

There are some other corners in this. They were trying to form a company around the uses of the organism. A very prominent figure in Silicon Valley wanted to form a company based on this technology, and only that company could use the organism. I remember meeting in Don Kennedy's conference room, and I said, "This is not right. This is something we want to make broadly available; this is a basic tool. By licensing it nonexclusively, I can get scientists throughout the world using the technology. Besides, if I can license the use of the organism nonexclusively, I think it's in the public interest that I do so."

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At any rate, before I began to put in all these arguments, Don had to go off to deal with a call that he had just gotten that Stanford apparently had a yacht, and that was in the indirect cost base. Do you remember that? By the way, I can explain. Stanford was not really guilty in any of this stuff, even the yacht thing.

Don didn't hear this, and I was really worried; I was upset. So I got together with Beyers and Spyros [Andreopoulos], and we had a private lunch meeting in Bob's conference room. And I said, "This can explode. I'm not going to sit back and be accused that I'm holding back distribution of this research result." That night, around eleven o'clock, I got a call from Beyers. He said, "I talked to Don. I got to him, and you've got a meeting with him at seven tomorrow morning." So I came in there at seven, and I told him this could be devastating.

Before Don had left the earlier meeting in his conference room, he said, "Let's find a way to make this work." And so everyone was leaning in that direction, except for me. So I told Don what I had said and my feeling that this was going to explode, and I wouldn't put up with it, and this is just not the way to do it. He fully agreed. And then later that morning, a press release went out that Stanford was making this organism and licenses broadly available. [laughter] I actually got in trouble for meeting with Don, because on my way back to my office, and by this time it was about eight o'clock, I stopped by Vice President Bill Massy's office. I said, "Bill, I just had a meeting with Don and wanted to let you know about this." He was upset that I didn't contact him first. I said, "Well, this was eleven at night."

### Hughes

When was this?

### Reimers

It was probably around 1980 or so.

### Reimers

I don't want to tell you too much to embarrass the inventor who has just died. It didn't work, actually. We still were going to pursue a patent, because the organism worked, but weakly. We chose to offer the companies that had paid for a license their money back. I had about seven licensees by then; four got their money back, and three of them decided to keep their license on the possibility a useful patent would result.

### Hughes

Well, I wonder if this letter is perhaps related to that episode.<sup>42</sup> It's dated November, 1980. You were writing to Kent Peterson. I don't know who he is.

### Reimers

He was my boss. I kept moving down in the organization. [laughter] Yes, this is it--Henry Kaplan, hybridomas. It was usually mouse-human or rat-human. Here he had a human fusion partner. It was Zaffaroni who wanted to put together the company, and he talked to Henry and then Don. I had no idea what was going on. I walked in the president's conference room, and there was Zaffaroni, there was Henry Kaplan, Don, a Stanford lawyer, and others. Henry hadn't advised me of his company plans. Does my memo to Peterson reflect which article I was referring to?

### Hughes

Well, there's one attached.

---

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### Reimers

Yes. [reads it] I look back and I don't fault what I did. That's satisfying.

### Hughes

I was interested in this part--may I quote it? You wrote this in the context of the hybridoma and the recombinant DNA research--maybe everything.

### Reimers

Yes, in general.

---

— [Begin Tape 3, Side A] ## —

### Hughes

November 18, 1980 memo to Peterson:

As Stanford is perhaps the first institution to begin filing genetic engineering patent application and to license hybridomas, we ... are to a degree "leading the way" for other universities and government policy makers. We need to be *very careful* in our public and private actions with respect to developments in these fields, including policies of cell line distribution and licensing so that we do not inadvertently, in fact, restrict scientific collaboration and deny or delay development of benefits of this research for the public. We must also guard against "overreaching" in financial and other license terms.

### Reimers

Beautiful.

### Hughes

There it is in black and white.

### Reimers

Yes, in black and white. I didn't realize I had done that. But by that time there were layers of people between the president and those doing the work. And I think there was sort of a loss of touch. Don's legal advisor built up a legal office from zero to somewhere around thirty lawyers, with a total staff of sixty or so.

### Hughes

Largely because of the patent situation?

---

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### Reimers

No, just because. Lawyers began to sit in in most important Stanford meetings, including licensing, and actually wanted to control us. And I resisted. They wanted to authorize all the patent filings that we made with private patent attorneys. I said that adds a layer of cost that's unjustified, we had never screwed up in any legal steps, and so we got out of it. Then they began to off-load part of their budget on us, as they did elsewhere, because they had to somehow pay for this large office, and we and other Stanford offices were going to pay for it. But to Gerhard Casper's credit, he cut the number of lawsuits way back, down to three or four or so. How many lawyers did MIT have? [Reimers forms a zero with his thumb and forefinger]

## A Possibility of Premature Disclosure

### Hughes

Well, I'm back to challenges to the validity of the patent after it issued in 1980. The *Biotechnology Newswatch* in 1982 reported that an article by Edward Ziff in the *New Scientist* in October '73 might count as premature disclosure.<sup>43</sup> Why was this an issue in 1982 when the process patent had already issued?

### Reimers

What they're saying is that there was that summer [1973] Gordon conference where Boyer first disclosed what he and Stan had done. You know there's a time lag before publication, so the publication hadn't occurred. The Gordon conference was supposed be an open exchange, and you're not to take advantage of someone else's discovery, in terms of beating them to publication.

Each Gordon conference focuses on a narrow field. They're usually held at a prep school back in New England, and it's just an open discussion. So one of the attendees may have told something to Ziff. But there's a question of what Ziff put in his October article as to what is called "enablement" in patent terms. I don't even remember this, by the way. If he mentioned what Boyer presented at the Gordon conference, the question is whether the Ziff article was really an enabling disclosure. If it were, he would have screwed us. Obviously, it wasn't, or somebody would have picked it up.

### Hughes

Why was this being debated in 1982?

### Reimers

I don't know if it was being debated, but they probably thought that that meant the patent was invalid. And if it was invalid, you can bet your boots the pharmaceutical companies that were paying royalties would have ceased immediately.

## Selling Licenses

### Hughes

We talked about the trips that were made in the fall of 1981 in which you were selling the technology or explaining the technology to companies that you thought might be interested in licensing it.

### Reimers

Well, Andy Barnes did most of that.

### Hughes

Do you know what kind of reception he got in most cases?

### Reimers

Andy is a vice president of Mycogen in San Diego; you could talk to Andy. We also mailed out a lot of stuff. We just sent letters out to everybody. Yes, Andy's marketing led to a career in the biotech industry. I actually released him early because he had a job offer he wanted to take. So I said okay, with tears in my eyes.

## The University Licensing Pool for Technology

### Hughes

One last question, in 1983, Stanford and UC formed the University Licensing Pool for Biotechnology.<sup>44</sup>

### Reimers

Oh, that was my proposal; it never went anywhere. What I was concerned about is, here we have a unique point in the history of technology where you've got this whole new field; you've got a basic discovery, and all of these other patents are coming up and being filed everywhere. So assuming they were all needed, they would be layered. It could be chaotic for companies to develop products because they'd have to pay Stanford; they'd [also] have to pay this university or that, and then another technology comes up from the university. I think I was a little over-concerned then.

The idea was that we would make available this pool of technology, except for the recombinant DNA patent. My friend, Howard Bremer at the University of Wisconsin, said, "You should include recombinant DNA." I said, "No." You put it into a pool, and maybe we included--oh I forget what I had--a 3 percent royalty. And companies would get all of this pool of patents, so it wouldn't inhibit them; they would get it nonexclusively. These would all be what I call "tool patents." A patent for an application, such as a specific drug composition, would not be included. Then at the end of the year, with input from the companies, we would establish the relative contribution as to which patents in the pool they were actually using and which ones they weren't. The patent pool concept died for lack of my enthusiasm and others'.

### Hughes

Well, that's the end of my questions. Do you have anything more you want to say?

### Reimers

Well, there are all sorts of little things that happened along the way. I'm pleased to see that somebody is interested; this is great. And then to see some of the words that I wrote a long, long time ago was kind of fun, sort of a personal retrospective.

### Hughes

Well, I thank you.

## Notes

1. ## This symbol indicates that a tape or tape segment has begun or ended. A guide to the tapes follows the transcript.
2. Reimers' editorial note: FY 96-97 income was \$52 million.
3. Victor E. McElheny. Gene transplants seen helping farmers and doctors. *New York Times*, May 20, 1974, 60:1.
4. An oral history is in progress with Stanley N. Cohen, which will eventually be available for research at UCB and Stanford.
5. S. N. Cohen, A. C. Y. Chang, H. W. Boyer, and R. B. Helling. Construction of biologically functional bacterial plasmids in vitro. *Proceedings of the National Academy of Sciences* 1973, 70: 3240-3244.
6. Reimers' note in editing: Dr. Helling was on sabbatical from the University of Michigan in Herb's lab. Because he was listed as an author, the University of Michigan contacted us, maintaining he was an inventor and that the UM was entitled to a royalty share. This was later resolved--only Stan and Herb were inventors.
7. BC [Bill Carpenter] to 74-43, September 18, 1974, re Dr. Herbert Boyer (Office of Technology Licensing, Stanford, S74-43, Correspondence 1974-1979. Hereafter, OTL correspondence.)
8. According to Swanson, Boyer and he first met to discuss the formation of a company, later named Genentech, in January 1976. See the oral history with Robert A. Swanson in the Program in the History of the Biological Sciences and Biotechnology Oral History Series. Hereafter, The Bancroft Library Series.
9. In the U.S., inventors may file a patent claim up to one year after public disclosure of the invention. European countries operate under a "first-to-file" patent system.
10. Memo, Bill Carpenter to Niels Reimers, S74-43, Gene Transplantation, and attachment, The Plasmid Gene Transplantation Technique, October 18, 1974 (OTL, Stanford, S74-43, correspondence 1974-1979.)
11. Mr. Reimers is mistaken about the handwriting; he refers to a marginal note penciled by the interviewer.
12. "In confidence, re: Process and composition for biologically functional DNA chimeras--Cohen-Boyer," July 1, 1975 (OTL correspondence 1974-1979.)
13. For a record of one such meeting see: John Poitras to File S74-43, Meeting on DNA Patent, May 17, 1976, attendees: Clayton Rich, William Massy, Robert Rosenzweig, Paul Berg, Stanley Cohen, Joshua Lederberg, William Baxter, Peter Carpenter, John Poitras. (OTL correspondence 1974-1979.)
14. See the oral histories with Paul Berg and Arthur Kornberg in The Bancroft Library Series.
15. For more on DNAX, see the oral history with Arthur Kornberg in The Bancroft Library Series.
16. United States Patent 4,237,224, Cohen et al., December 2, 1980. Process for producing biologically functional molecular chimeras.
17. See, for example: memo, Andy Barnes to Niels Reimers, September 1, 1981, Cohen-Boyer gene-splicing licenses (OTL correspondence 1980-1982.)
18. The Department currently has a Boyer Fund which largely supports students.
19. For Cohen's viewpoint, see his oral history in progress.
20. Memo, Niels Reimers to file S74-43, Recombinant DNA Process, July 13, 1976, subject: Licensing Plan (OTL correspondence 1974-1979.)
21. S. N. Cohen, A. C. Y. Chang, H. W. Boyer, and R. B. Helling. Construction of biologically functional bacterial plasmids in vitro. *Proceedings of the National Academy of Sciences* 1973, 70: 3240-3244.

22. Memo, Ken Imatani to Niels Reimers, subject: S74-43 Industrial Markets for Recombinant DNA Process, August 13, 1975 (OTL correspondence 1974-1979).
23. Memo, Ken Imatani to Niels Reimers, subject: File S74-43 Discussion with Dr Boyer for Future Development Work for Recombinant DNA Process, August 6, 1975. (OTL correspondence 1974-1979).
24. Unsigned penciled notes, probably by Reimers, dated April 9, 1976 (OTL correspondence 1974-1979).
25. Memo, Stanley N. Cohen to Niels Reimers, subject: DNA Cloning Patent, June 14, 1976 (OTL correspondence 1974-1979).
26. Memo, Niels Reimers to Robert Rosenzweig, subject: Recombinant DNA, June 18, 1976; memo, Robert M. Rosenzweig to Stanley N. Cohen, July 7, 1976 (OTL correspondence 1974-1979).
27. Memo, Niels Reimers to Robert Augsburger, subject; Recombinant DNA, July 19, 1976 (OTL correspondence 1974-1979).
28. In 1986, the American Chemical Society awarded Stanford and the University of California its ACS Award for their "innovative cooperative licensing of recombinant DNA technology." The paper (on the licensing of DNA technology) which Reimers refers to is: Niels Reimers. Tiger by the tail. Chemtech, August 1987, 464-471.
29. James D. Watson and John Tooze. The DNA Story: A Documentary History of Gene Cloning. San Francisco: W. H. Freeman and Co., 1981, p. 499.
30. Niels Reimers. Tiger by the Tail.
31. Massy to Rosenzweig, subject: Recombinant DNA Patent, March 2, 1978. (OTL correspondence 1974-1979.)
32. See the oral history with Arthur Kornberg in The Bancroft Library Series.
33. For discussions of DNAX, a biotechnology company in Palo Alto of which Berg and Kornberg are founders, see their oral histories in The Bancroft Library Series.
34. Tiger by the Tail.
35. See the oral histories with Arthur Kornberg and Paul Berg in The Bancroft Library Series.
36. For the foundation and development of Genentech, see the oral histories with Robert A. Swanson in The Bancroft Library Series and Herbert W. Boyer in the UCSF Biotechnology Series.
37. David Dickson. Inventorship dispute stalls DNA patent application. Nature 1980, 284: 388, April 3, 1980.
38. J. F. Morrow, S. N. Cohen, A. C. Y. Chang, H. W. Boyer, H. M. Goodman, and R. B. Helling. Replication and transcription of eukaryotic DNA in Escherichia coli. Proceedings of the National Academy of Sciences 1974, 71: 1743-1749.
39. On August 3, 1981, Stanford announced the recombinant DNA technology licensing effort: Advance for release August 3, 1981, Stanford University News Service (OTL, Stanford, S74-43, news clippings 1981-1985); "For immediate release," Stanford University News Service, November 17, 1981 (OTL, 74-43, news clippings 1981-1985). The first sentence reads: "Stanford's unprecedented effort to license the entire genetic engineering industry for use of its basic scientific techniques is off to a strong start..."
40. Dec. 6, 1980 news release.
41. For a report on and participants at the conference, see: Barbara J. Culliton. Pajaro Dunes: The search for consensus. Science 1982, 216:155-158.
42. Reimers to Peterson, subject: Cell Line Distribution, November 18, 1980 (OTL correspondence 1980-1982).
43. Patent office suddenly withdraws second Cohen-Boyer patent. McGraw-Hill's Biotechnology Newswatch, July 5, 1982, 1-2.
44. Marjorie Sun. A one-stop shop for gene-splicing patents. Science 1983, 219:1302-1303. For more on the Licensing Pool, see the appendix.

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