Title
Documenting the Biotechnology Industry in the San Francisco Bay Area

Author
Chandler, Robin L.

Publication Date
1997

Peer reviewed

Documenting the Biotechnology Industry In the San Francisco Bay Area

Robin L. Chandler
Head, Archives and Special Collections
UCSF Library and Center for Knowledge Management
1997

Table of Contents

Project Goals

The University of California, San Francisco (UCSF) Library & Center for Knowledge Management and the Bancroft Library at the University of California, Berkeley (UCB) are collaborating in a year-long project beginning in December 1996 to document the impact of biotechnology in the Bay Area. The collaborative effort is focused upon the development of an archival collecting model for the field of biotechnology to acquire original papers, manuscripts and records from selected individuals, organizations and corporations as well as coordinating with the effort to capture oral history interviews with many biotechnology pioneers. This project combines the strengths of the existing UCSF Biotechnology Archives and the UCB Program in the History of the Biological Sciences and Biotechnology and will contribute to an overall picture of the growth and impact of biotechnology in the Bay Area.

Project Methodology

Working directly with scientists, members of industry, university policy makers, historians, and sociologists to identify patterns of scientific collaboration between academia and industry, the archival staff will examine the scope of information produced by university scientists and industry, identify valuable types of information to preserve, and recommend future actions for the preservation of documentation. The model developed will suggest the preservation of records which illustrate relationships between University of California faculty and the biotechnology industry in the development and transfer of scientific ideas, the formation of companies, and in advisory roles to industry.

Products

- Specific archival appraisal guidelines for biotechnology papers and records to be used by archivists for selecting records
- Identification of specific papers and records for UCSF and UCB to collect from academia and industry
- Project recommendations to UC systemwide and industry for actions needed to document the impact of biotechnology on the Bay Area and the state
- Recommendations for continued collaboration between Berkeley and San Francisco in biotechnology
- Business model to fund continued joint biotechnology efforts

Participants Interviewed during 1997

Chiron:
Herbert Lee, Director Professional Services
George McGregor, Director of Information Services
Edward Penhoet, CEO
Martha Truett, Chief Forensic Scientist, Director Legal Information Services

Cooley, Godward:
Fred Dorey (formerly Director of the Bay Area Bioscience Center)

Genentech:
Buffie Fenner, Scientific Collaboration Materials Transfer
Irene Loeffler, Manager Records and Image Management
Barb Messer, Director of Information Services

UC Administrators
Suzanne Huttner, Director UC Biotech Systemwide
Charise Yarkin, UC Biotech Systemwide - Statistics

UC Berkeley Scientists:
Alex Glazer, Chair Molecular Cell Biology (MCB)
Daniel Koshland, Professor MCB
Gunter Stent, Professor MCB - Life Sciences
Robert Tjian, Professor MCB & co-founder of Tularik

UC Berkeley Scholars:
Roger Hahn, Chair History of Science & Technology Program
Jack Lesch, Professor History Department
David Mowery, Professor Business School
Paul Rabinow, Professor Anthropology

UCSF Scientists:
Leslie Benet, Chair Pharmaceutical Chemistry & founder of AvMax
Anthony Hunt, Professor Pharmaceutical Chemistry
Keith Yamamoto, Chair Cellular and Molecular Pharmacology

UCSF Administrators:
Karl Hittleman, Associate Vice Chancellor Academic & Research Affairs
Neils Reimers, Former Director Office of Scientific Management

I. Documenting Biotechnology in the San Francisco Bay Area

1. The Emergence of an Industry

On December 2, 1997 the patent for the discovery of recombinant DNA expires, and the gene splicing tool developed by Stanford University's Stanley Cohen and UCSF's Herbert Boyer becomes available for use within the biotechnology industry without licensing restrictions. In November 1997, on the eve of this event, the University of California San Francisco announced the selection of the architecture firm Machado and Silvetti to design the new Mission Bay Campus near downtown San Francisco. Clifford Graves, president of the Bay Area Life Sciences Alliance (BALSA) envisions the new facility as a "cutting-edge biotech education and research facility that also has adjacent land available for life sciences companies - so their close proximity will allow them to reap the benefits of collaborating with the University as well as with each other. "[1] This transfer of technology and ideas between the University and industry, life sciences research and the biotechnology industry will spur scientific discovery, economic development, and employment opportunities.

The biotechnology industry has become a significant economic force throughout the nation. Locally, Northern California has become a center of bioscience research and productivity that includes ten Universities and Research Centers generating $ 541 million in annual bioscience budgets with over 16,000 employees, and 316 biotechnology companies producing over $ 5.6 billion in annual revenues and employing over 39,000 persons.[2] Two of the biotech industry's giants, Chiron and Genentech, founded by University of California faculty, in 1995 employed more than 4,000 Californians with combined payrolls of more than $ 260 million.

Biotechnology has played and continues to play an important role in medical therapy, crop development, and human gene mapping, as well as in developing laboratory instrumentation and computer programs widely used in biological research. "The San Francisco Bay Area is considered the premier center of bioscience and bioindustry due to the number and quality of research

---

[1]UCSF Public Affairs Office. Mission Bay Design Competition Exhibit Caption. November 1997.
[2]Northern California's Bioscience Legacy. A Publication of the Bay Area Bioscience Center [1991], p.30

professionals, university research facilities, proliferation of high tech companies, and the availability of venture capital. [3] " The combined efforts of researchers at the University of California and industry have achieved many biological milestones, such as engineering bacteria to produce human insulin, the creation of the Hepatitis B vaccine, and the recent research efforts to produce vaccines to combat the AIDS virus.

In 1988, the Association of Bay Area Governments stated "the existence and growth of Bay Area biotech facilities is related largely to the existence of major university research facilities at UCSF, Stanford and UC Berkeley.[4] " The incubation of new ideas and the possibilities of technology transfer are what make the University of California a magnet for new enterprises. However, the emergence of the biotechnology industry in Northern California has not occurred within a vacuum. There are precedents for collaboration between industry and academia throughout the nation such as the Research Triangle in North Carolina and the famous Route 128 which grew out of the juxtaposition of business and industry with the nearby universities of Harvard and MIT. "Massachusetts General Hospital, the largest Boston teaching hospital associated with Harvard University, was foremost among institutions to establish industrial partnerships."[5] In 1980, the German chemical firm Hoechst AG signed a contract with Massacusetts General to create a $68 million molecular biology center. The biotechnology industry is also developing internationally. For years, public distrust of genetic engineering in Germany has been fueled by the Green Party's environmental concerns. Since 1993, public opinion has changed, and in response, the German government streamlined laws regulating genetic technologies, and set up its own national genome program. The biotech industry, however, is not flourishing in Germany: "what they absolutely lack is a venture-capital-based biotech industry...the German drug industry invested in biotech companies in the United States rather than at home." [6]

Thus, although the roots of biotechnology in the San Francisco Bay Area can be found in the strong academic foundation, the emergence of

---

[3]Biotechnology in the San Francisco Bay Area. A Report of the Association of Bay Area Governments, September 1988, p.xi

[4]ibid , p.xii

[5]Krizak, Joan D., ed. Documentation Planning for the U.S. Health Care System. (Baltimore: Johns Hopkins University Press, 1994)

[6]Germany Joins the Biotech Race. Science, Vol. 274, 11/29/96, p. 1454

entrepreneurial scientists and the vital presence of venture capital has been essential to its development. According to Edward Penhoet, Chiron CEO, venture capital in the Bay Area was equally as important as the science. Venture capital resulting from the computer industry has existed in the area since the late 1960s. According to Penhoet, "if the Cohen/Boyer invention was the seed, and the good scientists in the area were the fertile ground, then the venture capital was the fertilizer." [7] To better understand the emergence of this vibrant industry, it is necessary to examine the forces which molded and shaped academia and industry since the mid-1970s. These include developments in government, academia, and business that have affected the biotech industry in general, and events and persons which have shaped the University of California, Genentech, and Chiron in specific.

2. Developments at the University of California since mid-1970s

According to Fred Dorey, former Director of the Bay Area Bioscience Center, two crucial policies formulated by the federal government have influenced the nature of scientific research in universities and have thereby given birth to the biotechnology industry. The first policy affecting the University has been the continual sponsorship of basic research in the academic environment by the National Institutes of Health (NIH). In the United States, peer review has been the basis of determining the funding for these sponsored projects, whereas in Japan and Germany research content has been directed by the government. The second major research policy affecting research in academia was the Bayh-Dole Act of 1980. This legislation fostered research for the public's benefit, and has resulted in universities licensing and commercializing scientific ideas that have given rise to a lucrative industry rooted in molecular biology. [8]
A recent article in *The Scientist* summarizes the impact of these two policies succinctly:

> "....the government provides crucial funding for basic biological research in universities, approving research proposals based on scientific merit and peer review.....university research, in turn provides the scientific basis for the development of life-saving medical products by biotechnology

[7]Interview Penhoet with Chandler 11/11/97
[8]Interview Dorey with Chandler 4/4/97

> companies.....through basic research financed by $80 million in NIH funds, technology transfer via licensed patents, scientific expertise, and invention of manufacturing technologies, as well as the creation of companies by entrepreneurs trained at the institution." [9]

It is clear that the mechanisms for transferring academic ideas to the business environment has stimulated the development of an industry based on the research tenets of molecular biology.

The Bayh-Dole Act:

Technology transfer -- the transfer of research results from universities to the commercial sector -- is closely linked to fundamental research activities in universities. The concept is said to have originated in a report, entitled "Science - The Endless Frontier," which Vannevar Bush wrote for President Truman in 1945. At that time, the success of the Manhattan Project had demonstrated the importance of university research to the national defense. Bush, however, recognized the value of university research as a vehicle for enhancing the economy by increasing the flow of knowledge to be used by industry through the support of basic science. His report became instrumental in guiding the federal government's policy to provide a substantial and continual increase in funding of research by the federal government. It stimulated the formation of the National Institutes of Health (NIH), the National Science Foundation (NSF), and the Office of Naval Research (ONR). Due to the success of these and other agencies, the funding of basic research is now considered a vital role of the federal government. Late in 1980, Congress and the Executive Branch determined that the public would be served best by a policy that encouraged the use of inventions produced under federal funding and which promoted the participation of universities and small businesses in the development and commercialization processes.

On December 12, 1980, P.L. 96-517, the Bayh-Dole Act, was enacted as federal law. Some of the Bayh-Dole Act's most important provisions to the emerging biotechnology industry have been the establishment of a uniform federal patent policy, the encouragement of universities to collaborate with commercial concerns to promote the utilization of inventions arising from federal

---

[9]The Scientist, Vol. 11, # 10, May 12, 1997, p.3 "Report Shows Basic Science Creates Jobs"

funding, and the ability for universities to choose to retain title to inventions developed through government funding.

The Bayh-Dole Act has been effective in promoting technology transfer by universities. Let us compare some statistics before and after the legislation. Between the decade of 1974-1984, eighty-four universities applied for 4,105 patents with 2,944 patents subsequently issued, compared with the single year 1992, in which 139 universities received 1,557 patents. As another means of comparison, during the years 1974-1984, 1,058 licenses were granted by universities, but during in the period of 1989-1990, 1,510 licenses were granted. Lastly, in 1986, 112 universities reported licensing income of $30 million, but during the two year period of 1989 and 1990, thirty-five universities reported an income of $113 million.[10]

David Mowery, Professor of Business and Public Policy at UC Berkeley, interprets the effects of the Bayh-Dole Act differently. Mowery suggests that Bayh-Dole's effects on universities active in patenting prior to 1980 were modest, however, much of the increase in total U.S. university patenting after 1980 may reflect the establishment of technology licensing offices at institutions that formerly did little or no patenting. Furthermore, Mowery argues, that "the effects of this major federal policy shift on faculty inventions and patenting were mediated by a change in the agenda of academic research toward biomedical inventions. This development in turn reflected shifts in the composition of federal R & D funding, changes in research opportunities, and a shift in the research agenda toward areas of direct applicability in industry."[11]

As a result of the Bayh-Dole Act, universities throughout the country have established Offices of Technology Transfer to oversee the patenting of new technologies by academic scientists and the management of this intellectual property through licensing agreements. Neils Reimers, former Director of the UCSF Office of Technology Management, describes the evolution of this approach within academia as the technical marketing model versus the lawyer driven program. Reimers was employed at Stanford University at the time Cohen and Boyer collaborated on the development of their gene splicing mechanism and was responsible for patenting the invention. Cohen-Boyer's recombinant DNA tool served as a catalyst to the biotechnology industry,

[10] MIT Website: http://web.mit.eduosp/www/coge/coge.html
[11]Proceedings of the President's Retreat - January 1997, p.34

however, it made patent history as well. In a letter to Reimers, George Frederickson, NIH Director, affirmed "that it was appropriate that universities should, in general, patent and license recombinant DNA inventions provided that industry licensees comply with standards set forth in the NIH guidelines."[12] According to U.S. law, inventions are protected for seventeen years from the time of patent issue, or twenty years from the time of patent filing. During the late 1970s, Reimers advocated a new model of technical marketing which emphasized the fruits of scientific collaboration, rather than the lawyer driven program which sought profits through claims on patent infringement.[13] With this model, the focus is on the output of the research, however, Reimers cautioned that the licensing agreements should never affect the nature of the research.

The Academic Scientist as Entrepreneur and the Evolution of Partnerships between the University of California and Industry

On January 30 - 31, 1997, UC President Richard C. Atkinson held a retreat at UCLA to examine the University of California's relationships with industry in research and technology transfer. Motivation for the retreat was twofold. Atkinson and the University of California recognized that during the past two decades university research with commercial applications had greatly expanded, particularly within the biotechnology industry. The University's mechanisms -- its policies and programs -- for working with industry could not cope with this explosion and required examination and modification. In addition, Atkinson recognized that the Universitiy's partnerships with industry would only increase in ensuing years.

In the mid-1970s, developments in recombinant DNA technologies made the basic research tenets of molecular biology commercially tenable overnight. However, the academic structure was not sufficiently prepared to transfer ideas to industrial products. "Entrepreneurial faculty like Bill Rutter and Herbert Boyer were way out ahead of the University and the academic community, but that is not the case now," states Karl Hittleman, Associate Vice Chancellor for Academic Affairs at UCSF, "the university is now evolving - it's got to. Two factors changed the university landscape: entrepreneurial faculty and the Bayh-

---

[12]Reimers, Neils. Tiger by the Tail. Chemtech, August 1987. p.32.
[13] Interview Reimers with Chandler 4/18/97

Dole Act , which obligated universities to pursue the benefits of their inventions in the private sector."[14]

Robert Tjian, UC Berkeley Professor in Molecular & Cell Biology and co-founder of Tularik, a biotech company, has seen great changes within the academic environment during the last two decades. "During the last twenty years, there has been a major shift in faculty attitude towards faculty associating with companies... the University of California now has its own systemwide technology licensing offices, and the mechanisms are in place to protect patentable ideas produced in the academic setting. Licensing agreements protect the use of a molecular structure -- or process -- this is the use of knowledge. This is different than what happened in the 1970s with insulin and Hepatitis B vaccine."[15]

Suzanne Huttner, Director of UC Biotech Systemwide, concurs with Dr. Tjian's opinion. Huttner sees current UC President Atkinson as fostering an environment for biotechnology industry relationships to grow and he is now urging faculty inventiveness for working with the patent process. "Initially, faculty, such as Robert Tjian, were strongly against the entrepreneurial role for the faculty scientist, but his views evolved as patent and licensing mechanisms within academia were strengthened. Ray Valentine, a UC Davis Professor, who founded Calgene in 1980, was severely criticized by members of the University for his entrepreneurial role. [In previous years] the University did not encourage entrepreneurial roles for scientists. It was called scientific misconduct. "[16] During the last few years, the University has evolved to more readily accept the relationships faculty has with industry, and at the same time, the University has developed a greater proprietary concern for its inventiveness. "Currently, the University is bringing lawsuits against graduate students who are walking off with intellectual property [such as] plasmid cell lines, " [17] according to Huttner.

The President's retreat resulted in proposed revisions to University of California regulations concerning relationships between the University and industry in areas of student education, the academic environment, copyright, conflict of interest, and the university patent and licensing program. Discussion and debate about these recommended policy revisions is underway throughout

---

[14]Interview Hittleman with Chandler 6/25/97
[15] Interview Tjian with Chandler 6/11/97
[16]Interview Huttner with Chandler 5/20/97
[17]Interview Huttner with Chandler 5/20/97

the University, at the administrative, faculty and student levels. Academic values will be core to discussions as a partnership is sought which furthers the university as a "source of free, open, independent, objective, disinterested and responsible inquiry aimed at the production of knowledge."[18] Gerald Dopplet, Professor of Philosophy and Director of the Science Studies Program at UCSD, advocates a "peer-deliberation model" for structuring partnerships between university and industry that balances the desires of university decision makers concerned with research funding, collaboration with industry scientists, and equipment access with those members of the university concerned with preservation of academic values. Dopplet's peer deliberation model advocates that agreements between the university and industry should consider the freedom and openness of scientific communication, objectivity and independence, technology-transfer and the public interest, and the credibility of the university.

Research in the Basic Sciences at UC Berkeley and UC San Francisco

In 1963, Dr. Edward Penhoet, current CEO of Chiron, completed his undergraduate course of study at Stanford University, receiving his B.S. in biochemistry. Penhoet had begun his academic career at Stanford in 1958, the same year that Arthur Kornberg and Paul Berg were recruited by the Stanford Medical School and Charles Yanofsky was recruited by the Stanford Biology Department. A stimulating environment for the young scientist, Penhoet emphasizes "my experiences at Stanford were very important to my career. Inexperienced youth was seated at the table with Noble prize winners - and the young students were treated equally - and allowed to participated in discussions - in fact encouraged, unlike the programs in Europe and Japan which are structured more like apprenticeships. " [19] During his course of study, Penhoet first met William Rutter, a biochemist on sabbatical from the University of Illinois working at Stanford. At about the same time, according to Penhoet, Wendell Stanley, the Nobel Prize winning virologist came to Berkeley to chair the biochemistry department and establish the Virus Laboratory. Stanley attracted young scientists like Gunther Stent, a bacteriophage researcher, to the

[18]Proceedings of President's Retreat. p. 44
[19]Interview Penhoet with Chandler 11/11/97

new Laboratory. States Penhoet, "it is within this context that Molecular Biology begins in the Bay Area, and these two campuses, Stanford and Berkeley, are the foci."[20]

According to Penhoet, critical mass in the basic sciences did not occur at UCSF until the arrival of Bill Rutter as Chair of the Biochemistry-Biophysics Department in 1968. "There were good people at UCSF -- Holly Smith, Julie Krevans, Julius Comroe, and now Bill Rutter -- and Rutter began to recruit people to work on genes -- gene structure and function. Keep in mind that the Cohen/Boyer gene splicing tool was great, but it was the environment -- the laboratory, the space to work, the salaries -- and the people -- Varmus, Bishop, Boyer, and Tompkins -- that were critical. The Cohen/Boyer invention landed in fertile soil -- there was just so much energy happening at UCSF." For the purposes of documenting the emergence of biotechnology in the Bay Area, it is crucial to examine the evolution of the basic science research at the two prominent University of California campuses - Berkeley and San Francisco.

UC Berkeley - Restructuring the Basic Sciences

During the post-WW II period, biology was badly organized at UC Berkeley. "There were departments for bacteriology, botany and zoology," according to Gunther Stent, former Chair of Molecular and Cell Biology at UC Berkeley, "but no biology was taught." [21] Stent relates that Wendell Stanley was a major figure, responsible for teaching biology at Berkeley, but there were several other noteworthy figures in the biological sciences, including Melvin Calvin, a chemist interested in genetic ideas, and Don Glazer, a physicist turned biologist. Wendell Stanley was brought to Berkeley in 1948 by Robert Gordon Sproul, then President of the University of California, to revive biochemistry. At that time, the medical school students enrolled at San Francisco did their pre-clinical training at the Berkeley campus, but since the 1930s, the departments of biochemistry, physiology, and bacteriology were weak. Sproul had been at the Rockefellar Foundation, a private supporter of medical research, and Stanley had received the Nobel Prize in Chemistry for his discovery of the tobacco mosaic virus. Stanley predicted that the "Virus Laboratory will be as world renowned as

[20] ibid
[21]Interview Stent with Chandler 10/14/97

is the radiation laboratory of Dr. E.O. Lawrence."[22] According to Stent, "the UCB medical biochemists resented Stanley, so, these biochemists were moved to San Francisco [in 1958], to Siberia. So, until Tompkins and Rutter came to San Francisco, biochemistry was weak at UCSF."[23]

Alexander Glazer, Chair of Molecular and Cell Biology at UCB, describes the science departments at Berkeley in the 1970s as "organized along classical lines. Departments were distributed, for example plant pathology had a department of botany, and plant physiology had a department of botany. Genetics was in the College of Natural Resources, Bacteriology was in the College of Letters and Science, and Virology was in the School of Public Health."[24] Unfortunately, this kind of organizational structure does not allow for quick adjustments to new developments. During the 1970s, with the invention of recombinant DNA and the increasing sophistication of instruments, UCB was not ready to participate in the new era of scientific discovery. As Glazer relates,

> "the faculty were aware, they were smart, good people, but their administration wasn't consonant - it couldn't adjust. In addition, new campuses were being constructed throughout the system, and Berkeley did not complete well for limited construction and maintenance funds in this context. For example, Life Sciences was a state of the art building in 1932, but in the mid-1970s it was not suited to modern biological sciences and 70% of the biological sciences were in that building. Another problem in the mid-1970s was recruitment. During this time, there was an explosive growth of medical school biological sciences, so the ability to recruit top-notch people depended upon the facilities you could provide."[25]

However, according to Glazer, Berkeley did have some very strong faculty, such as Dr. Daniel Koshland Jr. who took the initiative to improve the environment. "Koshland did something very fundamental; he effectively deployed existing faculty."[26] Koshland understood the UC Regents would not respond to a direct request for funding for three new buildings. Alternatively, he formulated a process by which faculty would examine critically the academic

---

[22]Creager, Angela. Wendell Stanley's Dream of a Free-Standing Biochemistry Department. Journal of Biology 29, 1996. p. 348.
[23] Interview Stent with Chandler 10/14/97
[24]Interview Glazer with Chandler 10/14/97
[25]ibid
[26]ibid

department structure, review current research directions, develop a twenty year vision and determine what resources would be required to achieve this vision. In 1981, working closely with Glazer and David Wake, then a professor in invertebrate zoology, Koshland polled scientific faculty to discuss the aforementioned criteria. The responses were compiled as a report in 1983 sponsored by Vice Chancellor Roderick Park and Chancellor Michael Heyman.

The report revealed that the present laboratory facilities were untenable, and that faculty desired to reorganize the biological sciences around emerging directions in biology, not departments. In addition, the report suggested that the faculty should be regrouped into more felicitous arrangements, and not reorganized into new departments. As a result, three ecumenical science structures, which cut across colleges, were created: Molecular Cell Biology, Integrated Biology, and Plant Biology. It was a political masterstroke, because no small departments were lost, they simply became subdivisions of the mega-departments. The report resulted in 175 million dollars for new construction and modification of existing buildings. The College of Natural Resources, School of Public health, and College of Letters & Sciences received two new research buildings in 1989, the Molecular and Cell Biology building and the Life Sciences Annex, and in 1994 the existing Valley Life Sciences building was entirely remodeled.

Gunter Stent describes the context of the UCB reorganization:

> "in the 1970s, Berkeley's facilities were very poor. The Life Sciences building was overrun with cockroaches. Barker Hall, the biochemistry building, was built very poorly in 1964. Stanley Hall was the Virus Lab, and dated back to the 1950s. It was extremely difficult to get funding from Sacramento state government for new buildings. The state government had to be persuaded that Biology needed to be organized around new lines of research, and Alex Glazer was very successful at selling this new direction. At that time, it was difficult to get money for new buildings, so to get funding for buildings, you had to base it on a good reason." [27]

Alex Glazer states, "knowing three new facilities were to be put up, all the recruiting problems went away, so from a declining establishment, Berkeley has

---

[27]Interview Stent with Chandler 10/14/97

resurfaced in three years with vibrant, star -quality individuals. So, if you build good facilities, you will bring the most creative people."[28]

UC San Francisco - The Emergence of the Basic Sciences

The University of California School of Medicine began in 1874 when the Toland Medical College of San Francisco merged with the University. The Affiliated Colleges of Medicine, Pharmacy and Dentistry were built on the San Francisco Parnassus site in 1898, and the original Medical College building was constructed with laboratories for basic research. However, external events would soon shape the future of basic science research at the campus. Following the disastrous 1906 San Francisco earthquake and fire, the San Francisco Department of Public Health set up emergency hospitals near the Affiliated Colleges, and inadvertently, these new teaching hospitals supplemented the medical school experience for students. As a result, faculty members approached Dean of Medicine D'Acona, urging him to persuade President Benjamen Ide Wheeler to transfer the first and second years of the medical school curriculum to Berkeley. The transfer of these courses across the Bay allowed for permanent hospital wards to occupy the research laboratories of the Affiliated Colleges, where clinical practitioners could be trained. The first UC Hospital opened in April 1907 in the School of Medicine building, and Dean D'Acona became the first superintendent of the hospital. Typifying this separation of research and clinical departments, Herbert Mclean Evans became chairman of the Anatomy Department in 1915, situated on the Berkeley campus. Evans became Director of the Institute of Experimental Biology in 1931, also located at Berkeley, where he collaborated with Kathryn Bishop to discover Vitamin E.

Subsequent construction at the San Francisco Medical School was limited to the clinical enterprises. In 1917, the UC Hospital was completed, in 1933, the Clinics Building was constructed, and in 1956 Moffitt Hospital and the Medical School Building was opened for use. While the formal basic science departments resided at Berkeley, research interests with clinical associations did begin to develop in San Francisco including the George Williams Hooper Foundation (1914), the Laboratory of Experimental Oncology (1947), The Cancer Research Institute (1948), the Laboratory of Radiobiology (1949), the Metabolic

[28]Interview Glazer with Chandler 10/14/97

Research Unit (1950), and the Cardio Vascular Research Institute (1957). In 1958, the UC Regents transferred the first and second year courses for the School of Medicine back to San Francisco, reuniting the entire medical school by returning the basic sciences, including anatomy, biochemistry and physiology. Later, in 1967, the Hormone Research Laboratory, directed and founded by Cho Hao Li on the Berkeley campus in 1950 moved to the San Francisco campus to continue research into the isolation and identification of the human growth hormone.

In the mid-1950s, the School of Medicine recruited Julius H. Comroe Jr. from the University of Pennsylvania to direct the Cardio Vascular Research Institute (CVRI). Comroe was a clinical physician with laboratory experience, as well as a maverick scientist who advocated interdisciplinary research. In 1964, Clark Kerr, President of the University of California concluded that molecular biology was one of the the fastest growing scientific fields. Influenced by Comroe, Holly Smith, Chair, Department of Medicine, and Burt Dunphy, Chair, Department of Surgery, Kerr endorsed the philosophy of interdisciplinary research at the San Francisco campus and approved the construction of new research facilities. Symbolizing this new philosophy, in 1966 two new research buildings were constructed, Health Sciences East and Health Sciences West, creating ample laboratory space for the basic sciences. However, funding to support the research in these laboratories would be needed as well.

In the post World War II era, biomedicine saw an increase in federal support for research in the basic sciences. At the UCSF this "soft money" support helped bring about significant changes in the academic research environment of the University. One of the most significant of these developments was the rise of a restructured Department of Biochemistry and Biophysics. Under the direction of Chairman William Rutter, this department was transformed in the 1970s from a traditional medical school department into an active research unit at the forefront of molecular biology. It was here that in 1973 biochemist Herbert Boyer, together with Stanford University colleague Stanley Cohen, revolutionized biology by inventing recombinant DNA technology and plasmid vectors, making possible the manufacture of such artificial substances as growth hormone and insulin. Virologists Michael Bishop and Harold Varmus discovered that cancer-causing genes initially found in viruses are also found in humans, which was a major advance in understanding cancer, and this discovery would win them the Nobel Prize in Medicine. In 1979, John Baxter and Howard Goodman were the first scientists to clone the gene for human growth hormone, which became the second genetically engineered product to receive government approval. In 1982, based on research begun in his UCSF laboratories, biochemist William Rutter led the research departments at his biotech company Chiron to create the first genetically engineered vaccine against Hepatitis B. The UCSF Biochemistry and Biophysics Department's collaborative, interdisciplinary orientation served as the inspiration for several biotechnology companies, most notably Genentech and Chiron, and hence is fertile ground for exploring the process of translating basic science into clinical applications and marketable products in biotechnology.[29]

Opinion: Importance of Medical School Proximity to Basic Science Research

Alexander Glazer feels strongly that "the ground rules are same for all of biology, the receptors in insulin, and in the heart are similar across disciplines.....basic knowledge is the same. Study the rat, and you will learn about the human. You confirm your interpretation studies by experimenting with mice.....[these] model organisms drive biological research. [However], funding patterns have a much larger impact than where you are doing your research - at UCSF or at UCB. For example, Keith Yamamoto would be interchangeable with Robert Tjian. The National Science Foundation grants support for non-medical science - and this is about 20% of what NIH distributes in grants. At UCB the Integrated Biology research budget is 20% of what is at the department of Molecular Cell Biology per capita. Think of it this way, NIH funds Molecular and cellular research and NSF funds organism research. " [30]

3. Developments in Biotech Companies since mid-1970s

Creation of Genentech

In April of 1976, Herbert Boyer, a UCSF biochemist, decided to commercially apply the recombinant DNA techniques he had patented with Stanley Cohen of Stanford University to form the company Genentech. Boyer's partner in this enterprise was Robert Swanson, a young businessman with a degree in chemistry from the Massachusetts Institute of Technology and work

---

[29] Soft Money for Hard Science, lecture notes 11/12/97, Nancy Rockafeller, UCSF HHS Dept.
[30] Interview Glazer with Chandler 10/31/97

experience with the venture capital Kleiner, Perkins, Caufield and Byers. According to *Northern California's Bioscience Legacy* "Swanson was interested in commercially harnessing that technology, which some believed would effectively convert cells into factories capable of turning out drugs and other products."[31] Setting a pattern that became a industry standard, Swanson became the company CEO, and Boyer maintained his faculty position at UCSF, but served his company as a scientific consultant. With a small outlay of capital, literally only a thousand dollars, research resulting in the synthesis of the gene for somatostatin and the attached appendages for cloning the protein in the intestinal bacterium *Escherichia coli* was supported successfully at Boyer's laboratory at UCSF and in the laboratories of Keichi Itakura and Arthur Riggs at the City of Hope National Medical Center in southern California. With this success, Genentech, until then a company on paper, become a physical entity in 1977. As Arthur Kornberg describes it, " a laboratory was outfitted in an old warehouse in south San Francisco, where the nascent venture planned further to exploit the capacity of bacteria to become factories for the production of still other hormones, such as human insulin and human growth hormone, which could be put to immediate clinical use." [32]

A cloning race was underway at UCSF, as William Rutter's laboratory cloned the gene for rat insulin in 1977, and John Baxter and Howard Goodman's laboratory cloned the gene for human growth hormone in 1979. As a commercial entity, Genentech was in a position to quickly transform this scientific knowledge into medical therapeutics to promote human health including human insulin in E. coli (1978) and recombinant human growth hormone (1979). Genentech had attracted many bright young scientists, whose abilities ensured that Genentech would triumph in the early cloning races in the years 1978 - 1979. Among them were Dave Goeddel, formerly of the Stanford Research Institute, Alex Ullrich and Peter Seeburg, both former postdoctoral fellows at UCSF, and Arthur Levinson. "Upon announcing the cloning of the human insulin gene, Genentech was fortunate to have the endorsement of Eli Lilly, the company that had dominated the world market for bovine insulin [to] provide immediate financial assistance and gain the confidence of the investment community. Lilly's assistance improved Genentech's expression systems to

---

[31]Northern California's Bioscience Legacy (Oakland: Bioscience Center, 1991) p. 12
[32]Kornberg, Arthur. Golden Helix. p. 196

commercial levels and provided manufacturing facilities for a quality drug and applied the regulatory and related expertise that in 1982 , brought the first recombinant DNA drug [insulin] to market." [33] After cloning human insulin and human growth hormone, Genentech made its first public stock offering on October 14, 1980, and the market drove the price of stock from thirty-five dollars a share to a high of eighty-nine dollars. "It was one of the largest run-ups every of a newly traded public stock,"[34] and ultimately raised $ 39 million for the company.

Due to its wealth of creative scientists, Genentech was an overnight success, however, it could not sustain this momentum and direction. As a business enterprise, it grew rapidly, but the scientific research effort entered a period where it lacked steady leadership. Although a founder, Herbert Boyer had little daily influence on the research activities, preferring to exercise scientific guidance through Swanson and the Genentech Board of Directors. Some research efforts failed, as Genentech lost the races to clone alpha interferon and erythropoietin. From 1983 - 1989, David Martin, Professor of Medicine at UCSF with broad experience in biochemistry and clinical medicine, attempted to provide scientific direction for the company, however, the company was too distracted trying to manufacture and market the blood-clot dissolving drug TPA, and devoting energy to patent disputes, as well as regulatory hearings. In 1990, 60% ownership of Genentech was acquired by Roche of Basel, Switzerland for $2.1 billion, with options to purchase the remainder. Genentech, now a research division of Roche, was free from the concerns of clinical trials, manufacturing and marketing products, and able to concentrate on research science under the direction of Arthur Levinson. As a footnote, in 1991, Dave Goeddel left Genentech to form the biotech company Tularik, focusing on gene expression, with Robert Tjian, Professor in Molecular and Cell Biology at UCB, and Steven McKnight from the Department of Embryology at the Carnegie Institution. In addition, Axel Ullrich, after directing the Max Plank Institute of Biochemistry in Germany, returned to California to form the biotech company Sugen.

Establishing Chiron

---

[33]ibid., p.198

[34]Northern California's Bioscience Legacy (Oakland: Bioscience Center, 1991) p.12

In 1980, William Rutter, Chair of the UCSF Biochemistry and Biophysics Department was on the Scientific Advisory Board for Amgen, a biotechnology company on the verge of becoming an integrated pharmaceutical company located in Thousand Oaks, California. George Rathman, CEO for Amgen, explored with Rutter the possibility of opening an Amgen branch in the Bay Area. Rutter suggested that either of his two colleagues, Ed Penhoet, a Professor of Biochemistry at UC Berkeley, or Pablo Valenzuela, a Professor of Biochemistry at UC San Francisco, would be excellent candidates for the Director of Research for Amgen north. According to Penhoet, Rutter began "talking to Pablo and me about Amgen. Amgen would supply the funding, and the science would come from Rutter, Penhoet and Valenzuela, but there were concerns as to which branch, the north or the south, would be providing the leadership for the company. Out of these discussions we three decided to go it alone."[35] Bill Rutter brought the new company, Chiron, excellent scientific and organizational skills honed in academia and through experiences gained from consultantships with several pharmaceutical companies including Abbott, Eli Lilly and Merck. Penhoet's research interest was viruses, and infectious diseases, so the company's initial direction was vaccines and therapeutics. Vaccines also appealed to Rutter as the most strategic avenue for clinical application. With a mission to advance science and its application to medicine, the three founders chose Chiron, the centaur of Greek mythology, as the company's symbol. Renowned for his healing skills, Chiron instructed Apollo's son Asclepius, who became the Greek god of medicine.

With initial seed money of $ 900,000 from venture capitalist John Deleage of Burr, Egan and Deleage, Chiron was established in 1981 with Penhoet as CEO, Valenzuela as Director of Research, and Rutter as Chairman of the Board. According to Penhoet, the three founding scientists had good sized laboratories, with excellent post-docs to recruit as staff. They started Chiron with seventeen people in Emeryville, a location well placed between UCB, UCSF, and Stanford, and nearby to Cetus, an earlier biotech venture. Bill Rutter was already experienced in recombinant DNA technology from his experiences cloning insulin, and "he felt no hesitation about tackling the creation of a vaccine for Hepatitis B to be produced by yeast cells modified to function as vaccine factories. For a partner in this first Chiron project, Rutter turned to Roy Vagelos,

[35]Interview Penhoet with Chandler 11/11/97

a friend who had recently become the Director of Research at Merck ..... Vagelos had no interest in having Merck acquire equity in Chiron, but he was willing to transfer to Chiron the Merck funding already begun at UCSF for a genetically engineered Hepatitis B vaccine."[36] In 1982, the Chiron Corporation successfully developed the first genetically engineered vaccine for Hepatitis B. According to Penhoet, the founders were very cautious about acquiring funding for their company. Some of the early investors or partners in product development included Ciba-Geigy for research on somatomedins (growth factor) and Novo-Nordisk for research for single-chain insulin in yeast. These kinds of partnerships funded research at Chiron until 1983, when the company "initially offered public stock, netting $ 20 million.

Chiron acquired Cetus in 1991, after Cetus encountered serious fiscal troubles when the Food and Drug Administration failed to approve interleukin-2 (IL-2) a medical therapy for renal cancer. The purchase price for Cetus was $ 880 million, but by selling the Polymerase Chain Reaction (PCR) or DNA amplification patents to Roche, Chiron significantly reduced its actual cash payment to only $ 50 million. "After the purchase , unexpectedly, the Cetus product Betaseron (beta interferon) became a drug with enormous profit potential. Betaseron had failed in clinical trials as a therapeutic against cancer, however it worked to reduce the muscle spasms and paralysis of multiple sclerosis in a third of the patients it was given to. The FDA approved Betaseron in July 1993. " [37]

In November 1994, Ciba-Geigy, now known as Novardes since its merger with Sandos, invested $ 2.1 billion for a 49.9 % equity interest in a preferred partnership with Chiron. Today Chiron has five discrete business units which are diagnostics, oncology, vaccines, opthalmics, and technologies. According to Herbert Lee, Director of Professional Services, Chiron uses the principle of theramatrics in its work . "In this approach, you take a single medical problem and Chiron's goal is to develop tools for diagnosis (assay), means for prevention (vaccine), and the drugs for disease treatment (therapeutics)."[38] Two new Chiron products are currently being approved by the FDA, a Rabies vaccine and DTAP vaccine (portossis recombinant vaccine). Herb Lee states "Chiron considers

---

[36]Kornberg, Arthur. Golden Helix. p. 209
[37]ibid
[38]Interview Lee with Chandler 9/16/97

itself a small pharmaceutical company. The top three companies are Amgen, Chiron and Genentech. Amgen and Genentech focus on drug development, while Chiron also does diagnostics - it is the most diverse of the three."[39]

The Business of Biotechnology

Venture Capital

According to Barbara Immel, a biotech industry consultant with Immel Resources, "the average cost to produce a biotechnology product is 200 - 350 million dollars and takes an investment of seven to twelve years from research and development through manufacturing and clinical trials to get a product to market. The majority of the 1,300 companies currently in the United States are private companies, and they are not profitable."[40] In other words, there is no public stock available for purchase. Biotechnology is a very capital intensive business, and only 17% of small start-up companies have enough liquid assets to survive the long drug development period. Licensing has become a strategy employed by the biotech industry to bring revenue outside of sales into companies. If a company cannot develop a product sufficiently, the idea can be licensed to another company for completion. Because the cost of product development is so high, the current trend is towards mergers. Additionally, a new strategy has begun in the industry to develop a small company to the point where it can be sold. As a result, many biotechnology companies are either owned by major pharmaceutical companies, or a drug company has invested in the development of a specific product."

Biotech companies range in size from small companies who employ less than fifty staff, to top-tier companies whose employees number over 300 persons. Biotech companies can develop diagnostic and therapeutic products for human health care, research and produce agricultural products for use in microcrop protectants, plant genetics, food processing, and animal health, or they can produce supplies for the biotech industry including instrumentation, laboratory supplies and reagents. A top-tier vertically-integrated biotechnology company begins to resemble a small pharmaceutical company as it manages product

---

[39]ibid

[40]Notes from a lecture "Inside A Biotechnology Company," by Barbara Immell 9/25/96

development from its research through marketing stages. Departments in this size of a company include Research and Development, Manufacturing, Clinical Trials, Finance and Business Development, Quality Assurance, Patenting, Regulatory Affairs/Compliance, and Marketing.

The San Francisco Bay Area is home to a large venture capital industry which nurtured the high-tech electronic companies clustered in San Francisco and near Stanford University in Menlo Park, ultimately giving birth to Silicon Valley. With the founding of Genentech in the mid-1970s, investors began to develop an interest in biotechnology companies. "To meet biotechnology's need for long-term funding, company executives and investment bankers refined and adapted many traditional tools of corporate finance ..... biotechnology companies drew their funding from ..... venture capital, corporate partners, R & D partnerships and public stock and debt offerings."[41] Because of the long drug development period, and the necessary capital investment, bioscience funding usually begins with venture capital and graduates to corporate alliances or R & D partnerships for additional revenue. Only when a company reaches maturity and stability in its business enterprise and scientific program can a company offer stock for public sale. Corporate alliances are usually motivated by large pharmaceutical companies who desire access to a promising product or technology, and biotech companies who need cash investment to remain in business. Large pharmaceutical companies based in Europe are increasingly acquiring ownership interests in biotech companies. "Roche's purchase of its interest in Genentech ranks as the largest." [42] R & D partnerships often occur when biotech companies join forces to develop a specific product. In addition, some sections of the biotech industry have developed products with significant sales, making public stock offerings an important source for raising financing.

Economic Climate of 1990s

The business landscape for biotechnology companies is undergoing a time of dramatic change driven primarily by the lack of capital availability and the restructuring of the pharmaceutical industry. In this time of business turmoil "both biotechnology and pharmaceutical companies need partners to reposition themselves and to manage a new corporate environment. Big pharma [ceutical

---

[41]Northern California's Bioscience Legacy (Oakland: Bioscience Center, 1991) p.12
[42]Northern California's Bioscience Legacy (Oakland: Bioscience Center, 1991) p.14

companies] needs biotech innovations to replenish dwindling product pipelines quickly and efficiently. Biotech -- whose demonstrable strength has been drug discovery -- is availing itself of big pharma's capital and infrastructure." [43] Seeking creative means of financial investment, CEOs for some biotech companies are exploring alliance models where biotech companies could partner with academia for discovery, partner with CROs (clinical research organizations) for clinical and preclinical development, partner with pharmaceutical companies for marketing, distribution and sales, and even partner with other biotech companies for manufacturing.

The other dynamic driving infrastructural change for biotechnology companies is Wall Street's negative reaction to earlier industry promises. In the past, some biotech companies, eager to obtain financing, both through venture capital and public stock offerings, often made broad claims regarding their product's futures, heralding cures for cancer or AIDS. "These companies often rushed products with large market indications through early clinical development and into Phase III [clinical trials] in order to reap Wall Street's rewards, too often running into clinical disappointments. As a result, biotech companies now are having difficulty accessing sufficient capital resources."[44] Given this business climate, Barbara Immel believes consolidation, merger and acquisition will continue as the trend within the biotechnology industry. "The average survival rate for a lone biotech company will be approximately sixteen months, therefore, we will continue to see joint ventures and strategic alliances between pharmaceutical and biotech companies, biotech and biotech companies, and universities and biotech companies."[45]

Scientific Researchers in the Biotech Industry

According to George Mcgregor, Director of Information Services at Chiron, the corporate culture in his biotech firm reflects the vision from the top of the company. "Senior leaders believe science is good, and that with entrepreneurial faith, all is possible. At Chiron, the major players are scientists, they are the most important figures at this company. In some other companies, the MBAs -- the financial types -- have a lot of power, and at Chiron there are a

[43]Ernst & Young. Biotech 95: An Industry Annual Report, p. 37
[44]Ernst & Young. Biotech 95: An Industry Annual Report, p. 38
[45]Notes from a lecture "Inside A Biotechnology Company," by Barbara Immell 9/25/96

few lawyers who have leadership roles, but they are the exception."[46] Given this emphasis on scientific leadership, there is a heavily academic component to the corporate culture. Most of the personnel working at the company were hired from academic research and teaching positions, or the staff came from other segments of the biotech industry. The university subculture of molecular biology departments is prevalent in the company, which translates to an atmosphere of excitement, long work hours, pride in invention and the creation of new ideas, and a concern for mechanical aesthetics. "Also, there is an acute consciousness of costs associated with research and production. Chiron staff are sure UCSF will be functioning and contributing in the next century, but will Chiron? As more and more of the scientists employed at Chiron are also small businessmen, the model for the small biotech enterprise becomes the working model. This in turn generates a general belief in intellectual property, i.e. that a biotech or a pharmaceutical company does better at what they own."[47]

Robert Tjian, UC Berkeley Professor in Molecular & Cell Biology and co-founder of Tularik complements McGregor's analysis with this observation from the academic perspective. "At UC Berkeley, we train principal investigators (p.i.) to be creative thinkers ..... the industry approach to science has become the university approach to do good science ..... It is rare for a post-doc to chose a pharmaceutical company, but they will pick being a p.i. in a small biotech company or in academia. Pharmaceutical companies are big and bureaucratic - it is harder to maneuver scientifically. Size has an impact. Remember, large pharmaceuticals are good at manufacturing & marketing, but small biotechs are good at discovery and research. The model is developing where large pharmaceuticals sponsor research at small biotech companies. Economically this is like subcontracting - outsourcing. The brain power is in one place and the production is in another."[48]

4. Collaborations between Universities & Biotech Companies

Motives for Collaboration

[46]Interview McGregor with Chandler 4/21/97
[47]Interview McGregor with Chandler 4/21/97
[48] Interview Tjian with Chandler 6/11/97

In reviewing the nature of university-industry relations, there are several underlying motives for collaboration between the two organizations. On the university side, interests include "the potential for long-term support outside of government; help with financing sophisticated technology required for state-of-the-art teaching and research; access to specialized industrial equipment; support for graduate students; a broader and more relevant educational experience for graduate students; professional stimulation for faculty members; and potential marketing of university innovations with royalties returned to the university and individual faculty members. "[49] On the industry side, these interests include "access to highly trained graduate students as potential employees; access to competent scientists without having to develop extensive in-house capabilities; new ideas, approaches and products that enhance the competitive position of industry groups as well as individual companies; and improved capabilities for meeting government standards of environment, health and safety."[50]

While there are indeed motivating factors for collaboration, it is clear that the two institutions have fundamentally different objectives: academia versus business, knowledge production and dissemination versus profit. The university's greatest concern is the right to publish as opposed to industry's need to protect proprietary information. Additional conflicts result in areas where the perspectives of university and industry deviate including "program relevance, or what industry proposes versus what university can do; appropriate time frames; protection of proprietary information and patent rights and appropriate administration of licensing and royalty arrangements; and conflicts of interest."[51] It is these areas of conflict that necessitate the negotiation of appropriate contracts and licensing agreements to state the terms of business between the two organizations as collaboration occurs. As Robert Tjian observes, "UC has its own systemwide technology licensing offices, and the mechanisms are in place to protect patentable ideas produced in the academic setting. I have a number of patents with UC. Licensing agreements protect the use of a molecular structure or process. This is the use of knowledge."[52]

Funding of Academic Research by Industry

---

[49]Biotech and the Research Enterprise p.78

[50]ibid

[51]ibid

[52]Interview Tjian with Chandler 6/11/97

According to Karl Hittleman, Associate Vice Chancellor for Research Affairs, there has been an increase in funding from the private sector during the last few years at UCSF. In 1990, 26% of UCSF total funding came from private sector, however, in 1995, 37% of the campus total came from the private sector. Analyzed from another perspective, in 1990, there were 489 contracts from the private sector, and in 1995, there were 874 contracts. "That's an 80% increase during that time period. At the same time, there was a 17% increase in public funding between 1990-1995." Hittleman suggests that this increase in funding arises from the recent period of corporate downsizing, when pharmaceutical companies jettisoned their research divisions, and these companies strategized to contract with the university to use the academic research departments. However, Hittleman qualifies that "private funding is a contract - which means there is a deliverable product at the end, while public funding is a grant, which means there is no deliverable, it simply funds research." [53]

Concurring with Hittleman, Robert Tjian affirms that there is a mechanism to apply for grants from the NIH, but this is not the case with industry. However, he speculates that the administration for the University of California could develop a mechanism to attract corporate sponsorship from the pharmaceutical industry. "A technology transfer model that could be used in medical research could be industry sponsored positions in the academic laboratory - this would not be adjunct faculty or a p.i. from industry into the University. This model has got to be developed by scientists in the university who have had experience in industry....[and] has to be mutually beneficial. Education must meet its objectives of teaching and training, and industry must meet its objective of discovery." Leslie Benet, Chair of the Pharmaceutical Chemistry Department at UCSF, Chair of the UCSF Conflict of Interest Committee, member of the University Patent Board, and founder of the biotech company AVMAX developed a research sponsorship model based on equity. Benet brought the concept of equity to UCSF, after it had been successfully implemented at other universities. Benet's company AVMAX sponsors research at UCSF, and the university benefits by acquiring equity in the company and through patent licensing agreements as well. Benet's involvement with the Conflict of Interest Committee has greatly influenced his thinking, and he

[53]Interview Hittleman with Chandler 6/25/97

believes the equity benefit model is an ideal contractual relationship for sponsored research between universities and industry. "As a Department Chair you want to see interactions with industry, but you don't want to see these interactions become the driving force. This requires vigilance - it can get sticky."[54]

In 1985, the California State Legislature created the UC Biotechnology Program to foster and provide support to research in biotechnology, promote training at the UC campuses, and inform government, industry, and the public about developments in biotechnology. As part of this directive, UC President Atkinson initiated in 1995 the UC BioStar Project as a matching grants program to link UC scientists and California businesses in biotechnology research. A means of increasing private sector investments in university research and education at a time of unstable federal funding, the project promotes research into scientific areas and facilitates transfer of these solutions to the California economy, as well as establishing lasting linkages between biotechnology firms and UC scientists. With an expected length of two years, the grants range from $ 100,000 - $ 400,000, with the state and the industry sponsor contributing 50% to the approved project. University patent licensing revenues help fund the state's contribution to the research project. [55]

Types of Collaboration

When examining the types of collaborations academic faculty can have with the biotechnology and pharmaceutical industries, statistics reveal that 95% of the roles are consulting, ownership, representation of advisory boards, and expert witness, with the majority of faculty in consulting relationships with companies.[56] Leslie Benet consults with twenty pharmaceutical companies a year, and this department does the majority of consulting at UCSF. Benet states that at UCSF "the consulting money returns to the faculty member's laboratory to support the graduate students and post-docs. This is the ideal system and the motivation is to get financial support for the laboratory and not the faculty."[57] According to C. Anthony Hunt, Professor of Pharmaceutical Chemistry at UCSF,

---

[54]Interview Benet with Chandler 9/24/97
[55]UC Biotechnolgy Program website http://www.ucop.edu/uc_biotech
[56]Interview Tjian with Chandler 6/11/97
[57]Interview Benet with Chandler 9/24/97

"for faculty to consult with a company, the Department Chair must approve. The consulting agreement drafted by the company is sent to University, and the company reimburses the UC Regents for the consulting."[58]

In the UCSF Department of Pharmaceutical Chemistry, there are usually six to twelve adjunct faculty from the biotechnology industry working in the department, but this is the only campus department in which this occurs. Currently, there are seven adjunct faculty from Chiron and Genentech including Jeffrey Blaney (Chiron), Anthony Kossiakoff (Genentech), Frank Masiarz (Chiron), Walter Moos (Chiron), David Spellmeyer (Chiron), James Wells (Genentech) and Mark Zoller (Genentech). The adjunct faculty are not salaried faculty, but they are employees of industry recruited to lecture and direct thesis work for students. The University expects the individual to educate students and provide an opportunity for students to procure employment in industry after their graduate work. Adjunct faculty gain the benefit of new knowledge in the academic setting, however, the University does not expect the individual to act as a lens examining the department in detail. According to Hunt, thirty years ago, paradigm discoveries were made in academia, however, this figure has now dropped to about 50%, so 50% of the great discoveries are found in industry, therefore students benefit from the corporate source of knowledge. Benet describes the benefit slightly differently, "ideas flow across the industry and academic boundaries, so ideas and materials, like cell lines, are shared between the institutions."[59]

Working at Genentech's department for Research Contracts and Reagents, Buffie Fenner has a different perspective on collaboration between industry and academia. Responsible for all the outside work done with Genentech's proteins and cDNAs, Fenner oversees material transfer agreements, collaboration agreements, funded collaboration agreements and sponsored research agreements. According to Fenner, university scientists or post-doctoral student can legally contract to use Genentech proteins for experiments through material transfer agreements. Collaboration agreements formalize research between specific scientists at Genentech and at universities. This agreement is a negotiated document which outlines the work to be accomplished and the responsible parties. In addition, there are funded collaboration agreements

[58]Interview Hunt with Chandler 4/21/97
[59]Interview Benet with Chandler 9/24/97

which are similar to collaboration agreements, except that Genentech pays the university or organization for the conducted research. Lastly, there are sponsored research agreements that fund a specific academic scientist for specific Genentech work, and the company retains all rights to the discovery. [60]

Size of Collaboration

According to George McGregor, Director of Information Services at Chiron, collaboration with academic institutions is huge - UC Berkeley, UC San Francisco, and Stanford are heavily involved with research at Chiron. Publication is across the boundaries as well. "Rutter, the vision of the company, was Chair of the UC San Francisco Biochemistry and Biophysics Department and Ed Penhoet, the operations manager, maintains an association with UC Berkeley as adjunct faculty. Rutter is still deeply involved with endocrinology research at UC San Francisco. "[61] A search in the Dialog database Scisearch for the corporate authors Chiron, UC Berkeley, UC San Francisco and Stanford in the years 1985, 1990, and 1995 provides a statistical picture of collaboration between the Emeryville-based biotechnology company and the major academic research departments in the Bay Area. In 1985, the were a total of nineteen peer review articles published with these institutions as collaborators. As represented by those publications, 63% of the collaborations partnered Chiron with UC San Francisco, 10% of the collaboration partnered Chiron with UC Berkeley, and 5% of the collaborations partnered Chiron with Stanford University. The remaining 22% were cross-campus collaborations with Chiron. In 1990, there were a total of fifteen peer review articles published with these institutions as collaborators. As represented by those publications, 60% of the collaborations partnered Chiron with UC San Francisco, 13% partnered Chiron with UC Berkeley, and 20% partnered Chiron with Stanford University. The remaining 7% were cross-campus collaborations with Chiron. In 1995, there were a total of twenty-two peer review articles published with these institutions as collaborators. As represented by those publications, 59% of the collaborations partnered Chiron with UC San Francisco, 13% partnered Chiron with UC Berkeley, and 9% partnered Chiron with Stanford University. The remaining 19% were cross-campus collaborations with Chiron.

[60] Email Fennie with Chandler 9/29/97
[61] Interview McGregor with Chandler 4/21/97

A second search in the Dialog database Scisearch for the corporate authors Genentech, UC Berkeley, UC San Francisco and Stanford in the years 1985, 1990, and 1995 provides a statistical picture of collaboration between the South San Francisco-based biotechnology company and the major academic research departments in the Bay Area. In 1985, the were a total of twenty peer review articles published with these institutions as collaborators. As represented by those publications, 75% of the collaborations partnered Genentech with UC San Francisco, 10% of the collaboration partnered Genentech with UC Berkeley, and 15% of the collaborations partnered Genentech with Stanford University. In 1990, there were a total of thirty peer review articles published with these institutions as collaborators. As represented by those publications, 60% of the collaborations partnered Genentech with UC San Francisco, 13% partnered Genentech with UC Berkeley, and 23% partnered Genentech with Stanford University. The remaining 4% were cross-campus collaborations with Genentech. In 1995, there were a total of thirty-five peer review articles published with these institutions as collaborators. As represented by those publications, 57% of the collaborations partnered Genentech with UC San Francisco, 11% partnered Genentech with UC Berkeley, and 25% partnered Chiron with Stanford University. The remaining 7% were cross-campus collaborations with Chiron. The citations for these searches are available in Appendix A.

5. University Training Programs Preparing Students for Careers in Biotechnology

According to Neils Reimers, former Director of the UCSF Office of Scientific Technology Management, "students will be going into work in corporations, because there aren't many jobs in academia, and discussions are underway to develop a new program in academic life sciences at UC Berkeley and UC San Francisco to train students in how research is conducted in the private sector, and to develop skills in management and opportunity assessment."[62] The consensus among the research community is that more academic life scientists are being trained than there are jobs, industry will play an increasingly important role in funding academic research and the life sciences programs at the University of California have not yet developed formal

[62]Interview Reimers with Chandler 4/18/97

programs to provide students with the management and business skills they need to succeed in this new environment.

In an informal report prepared for Reimers, the UC Biotech Systemwide Office concluded that graduate students and post-docs have no established means of learning management skills associated with the successful direction of research labs during their academic training. In addition, UC faculty, post-doctoral students, graduate students and laboratory scientists occasionally discover potentially marketable new technologies, and these inventors could benefit from the opportunity to participate in a systematic multidisciplinary approach to market assessment and business plan development. There is a need to develop educational coursework focused on managing the scientific enterprise that would provide specific skills needed by life scientists who conduct business in academic or business sectors from research to transfer of technologies for development.

II. Appraisal Guidelines for Records Generated by Scientists in the University and the Biotechnology Industry

1. Why Preserve the Records of Biotechnology?

As policy makers, University Administrators are facing growing needs for information and advice in their decision making about biotechnology as this industry continues to grow in importance for the economic development of California. By providing information to state and federal legislators, university administrators help to shape and implement government policies that determine economic support for research in the field of molecular biology at the university level which ultimately evolve into the products of biotechnology. Preserving records concerning advances in molecular biology and the field of biotechnology will provide a rational foundation for decision making by the university and government at all levels. Additionally, University Administrators view the preservation of biotechnology papers and records generated by University academic researchers as protecting the resources of the institution and income generated through patents and licensing. By accurately documenting the research process and data produced a paper trail is provided through the legal maze of patents and licensing which can demonstrate the success or failures of research and development efforts.

While for most biomedical scientists, refereed journals preserve the history of their discoveries in molecular biology, there are several indications within the biomedical community pointing to a greater realization that measures must be taken to preserve broader documentation generated by significant projects. Hedrick in *Sharing Research Data* stated that these include wider opportunities for verification, refutation, or refinement of original results; the chance for replications with multiple data sets; encouragement of new questions and multiple perspectives employing the original data; the creation of new data sets through data file linkages; reductions in the incidence of faked and inaccurate results; dissemination of knowledge about analytic techniques and research designs; and the provision of expanded resources for the training of future scientists.[63] Echoing the final point, Keith Yamamoto, Chair of the UCSF Cellular and Molecular Pharmaceutical Chemistry Department, stated that the archived papers of scientists could be useful in the training of young scientists. "How the scientific community operates - how it acts - is crucial to success." In his course *Process of Science* Yamamoto presents real life situations that instruct young students in the ethics and etiquette of working as a scientist. Yamamoto believes that socialization is critical to a successful career, and that students must learn how to strike a balance between competition and sharing of information within the scientific environments of academia and industry. "Successful scientific research depends upon balancing the proprietary nature of information with public sharing of knowledge. Integrating archival documents with coursework would provide students with evidential role models for real life decisions."[64]

Researchers including historians, sociologists, policy analysts, business and legal scholars find the records and papers of biotechnology - the people and the institutions involved - to be a critical resource for understanding the process of scientific investigation, its results, and its impact. Archival resources in biotechnology can address significant scholarly questions including: How do discoveries in biological sciences become new medical technology? What are the major elements of the government-university-industry interface? What social and ethical issues do these alliances raise? What organizational features facilitate

---

[63]Fienbert et al. editors. Sharing Research Data. (Washington, D.C.: National Academy Press: 1985)

[64]Interview Yamamoto with Chandler 4/17/96

or impede significant scientific discoveries? Where does cooperation and competition occur within and outside the institutional setting? How has technology licensing been effected since the Bayh-Dole Act? What is the impact of the increased industry/academic relationship on the faculty environment? - Is the industry effecting the graduate students? Where does authority reside in the academic research process? What was the developmental trajectory of biotechnology that brought recognition to the University of California and was widely perceived as "progress." Given the presence of a medical school, the nearby Industrial Park, and the faculty recombinant DNA discoveries at Stanford University why doesn't the birth of the biotech industry happen at that campus? How did Paul Berg's conference to establish guidelines for genetic research held at Asilomar effect the entrepreneurial spirit at Stanford?

Biotechnology archival collections preserved in appropriate repositories will also provide centralized sources of information, essentially serving as the building blocks needed to create outreach programs for public education. Public understanding of the significance and importance of biomedical and ag-bio research is fundamental to maintaining government support for research institutions and subsequent technology transfer to industry. Ongoing public education can help to offset fears developed through alienation from the scientific process. Archival collections concerning biotechnology can promote access and public awareness especially through the use of digital technologies now fundamental to library and archives information distribution systems.

2. Research Records to Preserve

Scientific Research Process

The scientific research method is constructed of three major activities: administration, research, and dissemination. Research administration comprises three fundamental processes. Initially research priorities are established. A problem of study is chosen, the course of research is approved and political factors are considered. Funding becomes the next critical factor in project administration. Grant proposals are written, reviewed and approved. Finally, once the research direction is selected and funding assured, necessary staff is selected for the project. Research is the second major activity, and it is comprised of hypothesizing, planning the experiment and conducting the experiment.

Thinking and visualizing research outcomes are the first step. Sketching test procedures, gathering materials, and building and testing the research apparatus are the necessary planning steps for a successful experiment. Finally the experiment is conducted and the data produced is analyzed. Dissemination of experimental results is the final major activity of the scientific process. Findings are communicated and disseminated through oral presentations at conferences, and published as articles and reports. Conclusions are reviewed, critiqued, and diffused as work is cited, reused or refuted. Lastly, worthy inventions are patented as appropriate.[65]

These activities are reflected in the records produced by scientists. Memoranda, correspondence, and meeting minutes document the establishment of research priorities. Grant and research proposals, contract specifications, reviews of proposals, accounting records, final and annual reports document funding and allocation of resources. Curriculum vitae, annual performance reviews, publication lists, letters of recommendation, telephone lists or directories document staffing. Research notes, grant proposals, correspondence and memoranda document hypothesizing about experiments. Research protocols, work plans, interim and final reports, correspondence and memoranda, photographs, drawings and blueprints, operation notebooks, journal articles, technical reports, and instrument printouts all document planning and designing an experiment. Journal articles, progress reports, correspondence, annual reports, newsletters, photographs, and data records such as notebooks and electronic data all document conducting an experiment and analyzing the data. Journal articles, reprints, preprints, memoranda and correspondence, conference proceedings, slides and newsletters document the communication and dissemination of research findings. Memoranda and correspondence, disclosure forms, patent applications, technical drawings, illustrations, research notebooks, depositions and court transcripts all document patenting.

Types of Records to Preserve

Papers of Scientists

---

[65]Haas et al. Appraising the Records of Modern Science and Technology: A Guide. (Massachusetts Institute of Technology, 1985).p.20

Important unpublished documentation to preserve includes:

- scientific laboratory notebooks and research notes
- professional and personal correspondence, paper and/or electronic
- memoranda
- personal diaries
- electronic mail messages
- electronic research data
- research reports - progress, quarterly, annual
- grant applications, interim and final grant reports
- patent applications (conception to issuance), interference proceedings, infringement litigation
- meeting minutes & notes from committee meetings
- texts of presentations at meetings, lectures, symposia
- annotated preprints, reprints
- biographical or autobiographical materials
- photographs of the scientist, colleagues, laboratory, and instrumentation

Obstacles to Scientific Research Records Preservation:

There are two primary issues that provide obstacles to successfully documenting biomedical research in academia and industry and these are the legal nature of proprietary information and the tradition of reporting experimental results in journals and conference proceedings. "Competition alone dictates that information about proprietary discoveries not be shared with other organizations or individuals, at least until the data no longer have market value. Companies that have developed new drugs for the treatment of cancer.....find themselves under great pressure to justify decisions about the costs, marketing, and distribution of their products. They are certain, therefore, to be armed with policies concerning what they will disseminate to the public and what they will withhold."[66] Therefore, documenting the contributions of biotechnology companies by preserving the scientific record of their products will be difficult until the profit-making motive for a particular product, or process is no longer relevant. The second issue is more a "matter of philosophy and custom than legal substance .....t he traditional reliance on refereed journals as the primary medium for reporting and preserving the historical record of biomedical

---

[66]Krizack, Joan , ed. Documentation Planning for the U.S. Health Care System (Baltimore: Johns Hopkins University, 1994) p. 97

discoveries in the academic sector. For most biomedical scientists, journals are the true archives: at best, they convey succinctly the nature of discoveries, discuss their implications, and provide necessary directions for replicating experiments ..... it is no accident that the titles of well over one hundred biomedical serial publications representing a wide range of investigative fields begin with variations of the term archives."[67]

Scientific Records in Academia/Industry: Observations by Scientists & Professional Staff

According to Fred Dorey, former Director of the Bioscience Center, the Senior Scientist sets the tone - formal or informal - for each laboratory, and this will be reflected in the documentation produced and the interchange between researchers. Dorey believes the most important records documenting the scientific process are "personal laboratory notebooks which reveal the research process and the development of patents; drafts of reviewed papers, which contain the comments of other scientists, and reveal the ideas that shape a product; electronic mail and correspondence; and oral histories, because there is verbal exchange between scientists that goes into the development of an idea that never makes it on paper. " [68] Dorey has also observed two factors influencing the development of electronic information delivery in biotechnology companies. First, the Food and Drug Administration requires a detailed paper trail to monitor product clinical trials, and that this information is now submitted as electronic documents. Secondly, the Human Genome Database, an information tool for researchers in genetics is available through the internet. "Companies are using the web database for genome projects to produce genome sequences, however, they are not using the Web for a means of sharing communication about a project. In biotech, the scale is small, interpersonal communication is effective, and researchers don't need the web to communicate like physicists would around the globe. Email is more critical for sharing information in biotechnology collaborations."[69]

Les Benet, UCSF Chair of Pharmaceutical Chemistry, communicates mostly through paper distribution, but believes that this is both a product of his position as department chair and indicative of his generation. Benet believes his

---

[67]ibid
[68]Interview Dorey with Chandler 4/4/97
[69] ibid

post-docs and junior faculty are more likely to communicate by email. Benet also believes his published papers are the most important record of his scientific work, however, he notes that a lot of ideas are never recorded on paper, so these observations should be captured through oral histories. Benet states that at the University of California "a scientist signs a conflict of interest form, that clearly delineates where records have to be separated between industry and academia if you are working for both."[70]

Venture capital and the biotech industry are modifying the role of traditional publication formats. For example, *Science* magazine recently reported that in the industrial setting, the press release has replaced the scientific publication. "In the old days - say 2, or 3 years ago - breakthroughs in basic research were almost always announced at scientific meetings or published in peer-reviewed journals. No longer. Last week, Sequana Therapeutics Inc., in San Diego, issued a press release declaring that the company had "discovered the gene responsible for asthma." The three page press release contained little data of use to other researchers - such as where the gene is located, what it might do, or how many sufferers might carry it. Nor is anyone likely to find the answers in journals or at meetings anytime soon....it might be published within a year. The reason Sequana preempted the traditional scientific publication process has little to do with science. The announcement alerted investors that the discovery will earn the company a $ 2 million "milestone payment from Sequanna's collaborator, pharmaceutical giant Boehringer Ingelheim. Indeed, Sequanna's stock rose the day after the announcement...but at the same time...Sequanna doesn't want to disclose details until it has filed for a patent..." [71]

Robert Tjian, Professor at UCB Molecular and Cell Biology and co-Founder of Tularik, believes that email is prevalent in the scientific process, however, personally he prefers to conduct his work in paper, and his secretary screens electronic mail. Tjian does not envision a time when electronic notebooks will be used in biology. "Legally, I don't see digital notebooks being possible, paper, the hard copy, is the law. And remember, in biology, 80% of the work is done at the bench by an individual - its not like particle physics - where an electronic notebook is more useful because of the number of collaborators. Plus,

---

[70]Interview Benet with Chandler 9/24/97
[71]Science, Vol. 276. May 30, 1997, p. 1327

in biology an experiment may take eight to ten hours while in physics it may be eight to ten years."[72]

Keith Yamamoto, Chair of the UCSF Cellular and Molecular Pharmaceutical Chemistry Department, believes that laboratory notebooks are important to the scientist. Notebooks assist with misconduct problems; they provide a chronicle of the experimental work so that scientists can trace misconduct issues, and notebooks are useful for administrative legal needs concerning patents and licensing agreements. "Scientists recognize the value of these legal needs, but there really isn't a need to preserve the notebooks for science. If you need to reconstruct how a molecule is made, you just go back and redo the experiment. However, the legal issue is a real issue. Most scientists tell their post-docs to take their notebooks with them when they leave. However, if there were a systematic means by which to manage these notebooks, that would be very helpful."[73] Yamamoto notes that currently electronic information in molecular biology is confined to email and research data, however, academic scientists are on the cusp of electronic grant submissions and electronic journal submissions. Yamamoto observes that "the next generation of scientists will be "only" computer literate, and this could result in a time when laboratory notebooks are online."[74]

Irene Loeffler, Manager for Records and Image Management at Genentech, attended the Collaborative Electronic Notebook Systems (CENS) Consortium at the American Chemical Society (ACS) Symposium on Electronic Notebooks and Intranets on September 11, 1997. The Consortium was intended for scientists, engineers, attorneys, librarians, records managers, archivists, intellectual property specialists, information technology and laboratory automation experts in the chemical, pharmaceutical, biotechnology, agrichemical, food and beverage, oil and gas, consumer products, environmental, and related industries. According to Loeffler, the CENS Consortium envisions a "collaborative electronic lab notebook system" where teams of scientists worldwide can use to reliably capture, manage, securely share and permanently archive and retrieve all common data and records generated by Research and Development and testing labs. The CENS consortium's mission is to foster the

---

[72]Interview Tjian with Chandler 6/11/97
[73]Interview Yamamoto with Chandler 4/17/96
[74]Interview Yamamoto with Chandler 4/17/96

creation of open, commercially available, reasonably-priced and supported advanced software to support intra-enterprise research and development team project data management and collaboration, focusing short-term on complete electronic notebook systems that meet end user, and corporate scientific, patent, regulatory, and technical requirements. [75] Loeffler observes that among scientists at Genentech, there is some interest in electronic notebooks, but to become integrated into the research process there will have to be a demonstrated need.

3. Records Management at the University of California

In 1963, President Clark Kerr established a Records Management Program for the University of California, and appointed a University-wide Records Management Committee to coordinate the program at the campuses and at the Office of the President. The programs objectives include to assure economy and efficiency in the creation, organization, maintenance, use, and retrieval of administrative records; to promote sound records management practices; to establish and monitor a program of records disposition to assure that University records are not maintained longer than necessary, but are maintained as long as needed to meet administrative and legal requirements; to assure the protection of records vital to the University; and to ensure the preservation of records of historical importance.

The records disposition program was mandated to protect the University and its component parts by ensuring that all legal, historical, fiscal, and administrative requirements are satisfied before records are destroyed. In order to preserve records which document the history of the University of California, a University Archivist at each campus has been designated as the official custodian of all University records at that campus deemed worthy of preservation because of their historical value. Records schedules have been established in collaboration with the campus University Archivists, to ensure that records of historical value are transferred to the archivist for permanent retention. The University of California Records Disposition Schedules manage records produced through the administrative function, auxiliary and service enterprises, fiscal activities, medical functions, payroll, personnel and benefits functions,

[75] Interview Loeffler with Chandler 9/29/97

physical plant responsibilities, student admissions, registration and enrollment, and library functions as well as administrative electronic data.

The UC Records Disposition Schedules have little jurisdiction over the management of records generated by faculty during the research and teaching functions. Patent records including patent case files, licensing agreements, and financial records are managed by the UC Records Disposition program as are contracts and grants, however, there is no systematic method for handling faculty correspondence, email, and laboratory notebooks. It is common practice for individual campus University Archives and/or Special Collections to preserve, maintain and make available for access the papers of prominent faculty as appropriate to their collection development policies. For example, The Bancroft Library at UC Berkeley established in 1972 the History of Science and Technology Program which acquires the papers of faculty in the fields of science and engineering, manuscript collections with a special emphasis on early modern European and American science and technology, book collections with special strengths in early modern natural philosophy and mathematics, an oral history collection comprised of interviews with prominent UC faculty and Bay Area scientists, and the Program in the History of Biological Sciences and Biotechnology. The Archives and Special Collections at the UCSF Library and Center for Knowledge Management preserves and maintains unique materials to support research and teaching in the history of the health sciences for faculty and students across all campus disciplines. A major emphasis is the collection of archival materials in contemporary areas which correspond with research areas in the health sciences where UCSF has taken a leadership role including AIDS, Biotechnology and Tobacco Control. The department acquires the papers of health care professionals associated with the campus including current and former faculty and alumni. Rare published and printed resources form a major component of Special Collections with an emphasis on toxicology, homeopathy, high-altitude physiology, cholera and anesthesiology. In addition, the department maintains at East Asian Collection which emphasizes the historical development of medicine and the health sciences in China and Japan before 1900.

4. Records Keeping at Biotech Companies

Proprietary Information

"Discoveries in the industrial world far exceed the resources needed to pursue them. What matters most is making a shrewd choice of which discovery to develop, because each of the costly and time-consuming hurdles of clinical testing, regulatory approval, quality control and marketing is crucial in the success of a product ..... in the research and development expenditures of a pharmaceutical company, more than 90% is spent on development, whereas in academia, discovery with little follow-up can establish the discoverer's reputation. "[76] Because of the investment of time, staff, and capital required to produce a therapeutic, it is essential that biotechnology companies maintain their proprietary right to information about products developed by their company. A biotechnology company cannot afford to share research discovery when it takes ten years and $ 300 million to develop a new drug. In academia, scientists publish articles upon discovery, whereas in industry, scientists may publish, but only after ideas have patent protection. In the event of industry sponsored research in the academic setting, proprietary rights must be determined prior to the collaboration. Ownership of an idea must be determined prior to collaboration, or protracted litigation is probable after a successful research project. Because of the proprietary nature of information within the biotechnology industry, it is common practice to find company records management programs closely associated with the legal departments.

Records Management Programs

Chiron

At Chiron, Dr. Martha Truett, is the Chief Forensic Scientist and Director of Legal Information Systems. Truett's primary responsibilities include scientific support for the legal function, oversight and management of all information systems in use by the Chiron Legal Department, and administration of the records management for all records in the company. Truett provides scientific knowledge support for questions concerning intellectual property and litigation, especially patent prosecutions as needed. Managing all information systems in use by the Legal Department, Truett also oversees development and implementation of new systems as needed. For example, Chiron maintains a records management database and application for tracking all records held by

---

[76]Kornberg, Arthur. Golden Helix. p. 233

the corporation. Records management is important to Chiron, according to Truett, because records are necessary for litigation, and offsite storage of records is costly.

The development of retention schedules is a primary component of Chiron's records management program. States Truett, "this is a slow and ongoing process because there are limited staff resources for retention practices. The primary responsibility for records retention rests with each department, because the records creators know the importance and utility of the information [they create]."[77] Records Management staff meets frequently with research groups to review best practices to preserve records, determine organizational needs, survey records, and discuss the company's legal requirements for records retention. "The goal is to educate the scientists in research and development and staff in other departments, and to work with them to develop retention schedules ..... it [then] becomes the research group's responsibility to enforce the schedule."[78] This is a de-centralized approach to the implementation of retention schedules. Truett observes, "from a business perspective, Chiron has more leverage to persuade scientists to gain control over their records than a university does. When defending a patent in court, the scientists personal notebook is important - as are the supporting notes, correspondence, and memoranda."[79]

Another major focus of the records management program at Chiron, are the scientific research and development notebooks, all of which are checked out through the Records Management Group. Because they are the most important single group of records for patent defense, the notebooks are considered critical proprietary information. According to Truett, the research & development notebooks are all scanned to optical disk, and this data is available online and is retrieved through searchable fields. While the paper notebook is considered the permanent record, the optical version is used as a reference copy. Legal staff, records management staff and the scientists have access to the online version through IP addresses, but Truett observes "that often memories are best triggered visually, rather than by an online image. If individuals are searching for something, they often return to the original paper copy."[80] Chiron never

---

[77]Interview Truett with Chandler 9/15/97
[78]Interview Truett with Chandler 9/15/97
[79]Interview Truett with Chandler 9/15/97
[80]Interview Truett with Chandler 9/15/97

considered microfilm an option, because this media is location dependent upon a reader/printer, while the online version is available at the desktop computer. However, microfilm was used in several organizations that Chiron acquired over the past six years, therefore digital conversion of microfilm is in process.

Genentech

According to Irene Loeffler, Manager of the Records and Image Management, the Genentech Legal Department operates the corporate records retention program, and this is part of an overall effort to identify vital records in the company. Loeffler is responsible for managing the document imaging of laboratory notebooks and clinical trials records at the company. Loeffler states "that one of the company's major efforts is to microfilm the research notebooks, and this is an ongoing process. The notebooks run the spectrum; some experiments are well documented, legible, signed, etc., while others are quite the opposite. "[81] Once a scientist's personal notebook is microfilmed, the microfilm is stored in the Legal Department, and the original notebook is returned to the scientist or stored through the Records Management Dept. While paper records are still considered permanent, Loeffler noted that the legal system "will accept digital records as evidence, if that is all that exists, and if that is how the company does its business. "[82]

FDA Regulations

According to Steven Mendivil, Manager of Regulatory Affairs at Amgen, Inc. , the Food and Drug Administration (FDA) regulates the drug development process by monitoring the pre-clinical development and clinical development of therapeutics. During pre-clinical development or the research period, the goal is to predict potential adverse effects and design clinical studies that will minimize their occurrence. FDA regulations for the pre-clinical period help maintain good laboratory practices to ensure quality clinical protocols and qualified investigators. During clinical development of therapeutics, the objective is to demonstrate the product's safety and effectiveness. Clinical development typically involves three phases or trials. During Phase One, animal product

---

[81]Interview Loeffler with Chandler 9/29/97
[82]Interview Loeffler with Chandler 9/29/97

testing and initial human data is compiled to gauge general safety by determining what are the illicit responses and side effects of the drug. In Phase Two, limited effectiveness studies are performed to establish effective dosages for disease states. Small human populations are tested during this phase. In Phase Three safety and effectiveness is tested in specific populations. Typically these are hospital settings, where the dosage is tested on large populations of hundreds or thousands of individuals. Phase one - three can last from one to twelve years.

During clinical development two sets of FDA regulations monitor therapeutic development. These are good clinical practices, that define clinical trial-related responsibilities, and good manufacturing practices, that specify standards for manufacturing facilities to ensure product identity, quality, purity and strength. After the Clinical Trials are completed, a New Drug Application (NDA) is filed with the FDA for approval to sell and market a new pharmaceutical in the United States. The FDA reviews applications to determine if a product is safe and effective, if labeling is appropriate, and if manufacturing methods and quality control were adequate. Typical NDAs consist between 50,000 and 250,000 pages and consist of documents detailing manufacturing and quality control, clinical data, case studies and patent information. It generally takes over two years to review and approve a drug before it is available in the marketplace, but through the use of online application submissions, the FDA hopes to reduce the approval process to twelve months.[83]

At Chiron, Martha Truett observes that the largest volume of records are produced by Manufacturing and Quality Assurance, Quality Control, Regulatory Affairs, Pre-Clinical Trials, and Clinical Trials, and these are all departments whose functions are regulated by the FDA. "The FDA dictates guidelines for records necessary to preserve, but Chiron can decide on ancillary documents - beyond FDA guidelines to retain, and may keep FDA mandated records longer that the FDA requires. [Thus,] the Clinical Trials Group manages their own documentation, but the Records Management Group assists with development of retention schedules."[84]

Archives & History

---

[83]Inside a Biotechnology Company. Lecture on Regulatory Affairs/Compliance, by Steve Mendivil, 11/13/96.
[84]Interview Truett with Chandler 9/15/97

Martha Truett hopes that soon Chiron's records management function will include identifying historical documents created by certain groups for preservation. During our interview, Truett inquired about my purpose in visiting Chiron. In answer, I described the collaboration project's emphasis on encouraging companies to preserve documents for their archival value as well as the proprietary need for preserving documentation. In addition, I described how the development of the Hepatitis B vaccine occurred both at UCSF and at Chiron, and the history of this vaccine will be better understood by preserving research documentation within the university and the corporation. Additionally, I suggested that there may be means by which the university can assist with the preservation of historic documents. Ephemeral documents such as newsletters and annual reports could be preserved permanently by the University of California for Chiron and the public. Responding to my interest in ephemeral materials documenting the company, Truett observed that the maintenance of information about the company has been very spotty and would be preserved by Chiron Corporate Communications. The company has put out newsletters from time to time. Larry Kurtz, Head of Corporate Communications for Chiron has recently left the company, and Kurtz's replacement will inherit this responsibility. The Legal Department does maintain copies of all of Chiron's annual reports, as well as those reports from the companies Chiron has merged with over the years. Dr. Truett noted "that confidentiality for Chiron newsletters and other documents detailing work at Chiron would be an issue requiring resolution before University preservation of our documents could be considered."[85]

Irene Loeffler affirmed that there is knowledge of the company's roots, for example, a bronze statue commemorating the first meeting between Swanson and Boyer, and awards received by the company are mounted in the main lobby. Loeffler stated "she hopes that the company's administration is interested in the history of the company, but there is not a lot of funding available to support this."[86] In addition, Loeffler stated that Genentech Corporate Communications maintains the annual reports and newsletters for the company, and she believes

[85]Interview Truett with Chandler 9/15/97
[86]Interview Loeffler with Chandler 9/29/97

it would be appropriate to inquire about microfilming these ephemeral documents for the University of California Libraries.

III. Collecting and Preserving Records in Biotechnology

To finalize the strategy for documenting the emergence of biotechnology in the San Francisco Bay Area, it is important to consider potential users of the materials, the diverse nature of biotechnology and how that will influence what should be collected, and the records keeping practices of the creators of records, as well as additional partners for the collection effort. Therefore, the following includes: a brief overview of current academic scholarship intended to provide insight into potential users of biotechnology archives, a series of approaches to consider given the vast universe of biotechnology records, and a series of Project Recommendations are aimed at improving University records keeping practices, fostering the preservation of the historical record at local biotechnology companies, and encouraging the participation of the Stanford University Libraries in our project, as well as recommendations for documenting biotechnology at the Libraries of UC Berkeley and UC San Francisco.

1. Potential Users of Biotechnology Archives

Overview of Current Scholarship

Anthropology

Biotechnology and molecular biology research have recently become the subject of anthropological studies where researchers are examining the process of science in the modern world. Paul Rabinow, a professor of Anthropology at UC Berkeley, has recently written about Cetus, now a part of Chiron, where the polymerase chain reaction (PCR) technology was developed. Cetus scientist Kary Mullis won a Nobel Prize in 1993 for the development of PCR, and these efforts were chronicled in Rabinow's book *Making PCR: A Story of Biotechnology*. Rabinow continues to explore molecular biology with his new book underway, tenatively titled*French DNA* . This work is based upon his experiences as a philosophic observer at the genome-mapping center in Paris, France.

Business and Economic Growth

A line of inquiry in current business scholarship concerns the development of technology transfer policies by government for use in universities and industry. At the UC Berkeley Haas School of Business, David C. Mowery, professor of Business and Public Policy has long been interested in the transfer of technology, technology policies and the role of the government in fostering industry research and development. Recently, Dr. Mowery presented a paper " University-Industry Relationships: Historical and Policy Perspectives," at the President's Retreat concerning the University of California's relationships with Industry. Currently he is researching and writing a comparative technology licensing study examining patterns at Stanford University, Columbia University, and the University of California in conjunction with the emergence of the biotechnology industry.

Health Policy Studies

University-industry research relationships are becoming widely accepted and increasingly common in the life sciences, however, the impact of this influence has yet to be measured fully. David Blumenthal, a physician and public policy analyst at the Health Policy Research and Development Unit of Massachusetts General Hospital, and a professor at the Harvard Medical School, Boston has been examining these academic-industry research relationships or AIRRs, as he describes them, between academic scientists and genetics-based firms to determine their frequency, benefits, risks, and evolution. The results of his on-going research has been recently published by *Academic Medicine,* the *Journal of American Medicine* (JAMA), *Nature Genetics*, and the *New England Journal of Medicine.* In his article entitled "Ethics issues in academic-industry relationships in the life sciences: the continuing debate" published in *Academic Medicine* in 1996, Blumenthal argues that ethical reasoning militates against the involvement of scientists and universities in those AIRRs in which a financial conflict of interest on the part of life science investigators may affect the welfare of human subjects and trainees. In addition, he believes that scientists withholding data and redirecting research in commercial directions could undermine public trust in and support of university researchers. Ultimately, Blumenthal concludes that more research is needed on the harms and benefits of

AIRRS, and that it is prudent for universities and faculty to participate at modest levels in such relationships and to monitor them carefully.[87]

History of Science

In a 1995 issue of the periodical *Historical Studies in the Physical and Biological Sciences*, Pnina G. Abir-Am, a historian from Massachusetts Institute of Technology published a bibliographical essay outlining new trends in the history of molecular biology. Abir-Am wrote "there is much, however, to interest historians and their readers in the parent discipline of the biotechnology industry, and the mega-billion dollar projects centered on the human genome. Already there has been considerable public debate over social, legal, and ethical problems, real or imagined, about the projects and an increasing presence of themes from molecular biology in the cultural representation of science."[88] Abir-Am reviewed the recent works by historians of science actively writing about molecular biology including the *Histoire de la Biologie Moleculaire* by Michel Morange; *Molecular Politics: Developing American and British Regulatory Policy for Genetic Engineering* by Susan Wright; *Partners in Science: Foundations and Natural Scientists, 1900-1945*, by Robert Kohler; *The Molecular Vision of Life: Caltech, the Rockefeller Foundation and the Rise of the New Biology* by Lily E. Kay; *The Architecture of Proteins: Building the Laboratory of Molecular Biology at Cambridge/UK* by Soraya de Chadarevian; and *The Path to the Double Helix: the Discovery of DNA*, by Robert C. Colby.

Medical Sociology

A recent and important line of inquiry in the sociology of modern medicine concerns the relationship between the external environment of health care and the internal dynamics of the profession. Much of this attention focuses on the reorganization of the health care delivery system, the status of medical dominance, and the rise of new "elites" within the profession. Health care, once a cottage industry of solo practitioners and organizations, is now a market-driven system of highly diverse and increasingly, integrated and "managed" practice arrangements. The changes are driven by a broad range of social and economic

---

[87] Blumenthal, David. Academic Medicine, December 1996, 71 (2) 1291-6. Abstract.
[88] Abir-Am, Pnina. Historical Studies in the Physical and Biological Sciences, 26:1 (1995) p. 167

forces including the rise of consumer activism, public demand for medical care, advances in technology and therapeutics, the burgeoning corporate environment, capitated payment mechanisms, and government regulations. [89] The biotechnology industry, a developer of new therapeutics and delivery systems, is emerging within this radical transformation of the organization of health care and effecting its overall change and direction. Biotechnology companies and the pharmaceutical industry have been at the center of the development of AIDS therapeutics. In the mid-1980s, physicians and patients were enormously frustrated with the lack of scientifically grounded research on the benefits and harms of therapies for AIDS related illnesses. In 1987, non-academic clinicians at the Community Consortium of San Francisco and the Community Research Initiative of New York collaborated on a pharmaceutical industry sponsored clinical trial that resulted in the approval of the drug by the Food and Drug Administration. Medical sociologist Steven Epstein, a professor at UC San Diego has explored some of these issues of medical authority and the changing health care system in his recent work *Impure Science: AIDS, Activism and the Politics of Knowledge*.

2. Approaches to Documenting the Field of Biotechnology

Where does biotechnology begin? There are a multitude of ways to conceptualize biotechnology because simultaneously it represents inventors, basic science discoveries, commercial products, small companies and big pharmaceuticals, scientific processes, patents and licensing agreements, interdisciplinary research, government regulations, and academic policies. Reflecting the term's multiple meanings, a variety of approaches can be implemented to document the subject area. The following outline should be considered a point of departure. It will serve to foster the discussions between archival staff and advisory personnel at UC Berkeley and UC San Francisco as we finalize our collaborative plan to document biotechnology in the Bay Area. My collecting recommendations, based on this outline, will be found in Section Three Project Recommendations, Item D. *Biotechnology Documentation Effort By the Libraries of UC Berkeley and UC San Francisc*.o. The two campuses can choose another course to document biotechnology by reviewing the significant topics,

---

[89]Mueller, Mary-Rose. Unpublished Paper, 1996. "Medical Administrators and the Dynamics of Control Over Federally Sponsored Community-Based Research for AIDS." p. 2

specific products, certain organizational records, individual scientists, specific campus laboratories and research centers, important biotechnology companies, and by capturing the oral histories of individuals prominent in the field. These approaches are not mutually exclusive, therefore, a combination of approaches is recommended for appraising and selecting significant archival and manuscript sources necessary to document the emergence of biotechnology in the San Francisco Bay Area.

A. Significant Topics

Development of the NIH Guidelines on Genetic Engineering - Asilomar Conference

On July 26, 1974, Paul Berg, Stanford biochemist and Noble Prize winner in chemistry, drafted a letter that was published in *Science* and signed by prominent scientists including Stanley Cohen and Herbert Boyer proposing a voluntary moratorium on certain types of recombinant DNA experiments, and requesting that the NIH form an advisory committee to draft guidelines for genetic research, and to convene a meeting to discuss potential biohazards. This resulted in the Asilomar Conference focusing on biological containment which was held for four days on February 24 - 27, 1975. In June of 1976, NIH Director Fredrickson issued the NIH guidelines for genetic research based on discussions at Asilomar.

Foundation of Recombinant DNA Technologies

Arthur Kornberg discovered an enzyme, extracted from the common intestinal bacterium *Escherichia coli*, with the astonishing capacity to replicate DNA from any microbial, plant, or animal source. A few years later, in 1959, Kornberg received the Nobel Prize for Medicine shared with his former mentor Severo Ochoa for the discovery of the enzyme DNA polymerase. That same year, Arthur Kornberg left Washington University to establish the Department of Biochemistry at Stanford University accompanied by microbiologist Paul Berg. At about the same time, Charles Yanofsky joined the Stanford Department of Biological Sciences and Joshua Lederberg arrived from Wisconsin to start the Department of Genetics in the Stanford Medical School. With this leadership, Stanford became a training ground for future leaders in the field of molecular biology. Several years later, the splicing techniques for generating recombinant DNA were discovered at the Stanford Biochemistry Department by Paul Berg and his students using enzymes to cut, fill and seal breaks in DNA. Paul Berg's discovery was recognized in 1980 with the Nobel Prize in Chemistry which he shared with Walter Gilbert and Frederick Sanger, who had perfected techniques for determining the sequential order of nucleotides in DNA.

Discovery of Recombinant DNA and the Cohen-Boyer Patent by Stanford/UC

In 1973, Stanley Cohen and Herbert Boyer filed a patent for the use of recombinant DNA to clone genes in bacterial, plant, and animal cells. Issuance of the recombinant DNA patent, assigned formally to Stanford University, but shared with the University of California, acknowledged that the claims by Cohen and Boyer for the use of plasmids and restriction nucleases constituted a novel invention of DNA technology. With an annual license fee of $ 10,000 for access to the Cohen-Boyer patent, a vast number of biotech ventures have used the gene splicing tool to create products that extend and enhance human life. The patent income, shared equally between Stanford and the University of California, is expected to grow to $ 170 million by the patent expiration in 1997, the largest source of such income in the history of universities. The decision to patent the recombinant DNA technique and the breadth of the claims upheld by the Patent Office were widely noted by academia and industry. [90]

Race for Insulin

In May 1976, the Eli Lilly company held a meeting at corporate headquarters in Indianapolis inviting biologists and biochemists from around the country for a symposium on manufacturing insulin using genetic engineering. Invitations went to career researchers in the insulin field and prominent molecular biologists who were leading the way in discovering and applying new gene-splicing techniques. From UCSF, came Bill Rutter, head of one of the leading recombinant research groups in the country, and Howard Goodman, whose UCSF laboratory had teamed with Herbert Boyer on many projects in the forefront of the gene splicing field. From Harvard University's Biological Laboratories came the molecular biologist Walter Gilbert. Herbert Boyer, biochemist and co-inventor with Stanley Cohen of the gene-splicing technology, did not attend the Lilly meeting, because he had co-founded Genentech with Robert Swanson in April of 1976. Genentech's aim was to make a small human protein called somatostatin as a test project, then proceed to make insulin. Unlike the Gilbert and Rutter-Goodman groups, which were searching for a glimpse of the insulin gene and how it worked, the Genentech workers wanted to synthesize the human insulin gene and make human insulin as a marketable product. Synthetic insulin would be produced through the combined research efforts of these research competitors.

Creation and Evolution of the Biotechnology Industry:

---

[90]Kornberg, Arthur. Golden Helix, p..241

The birth of an industry could easily be documented by preserving the records for the founding of Genentech. In 1976, Recombinant DNA technology, harnessed by Stanley Cohen and Herbert Boyer, became the foundation of a viable business. Genentech's launching marked the beginning of what is today almost a $ 9 billion per year industry that includes more than 1,300 companies and more than 100,000 employees in the United States. Founded with initial venture capital of $ 1,000, Genentech today has a market capitalization of more than $ 6 billion and assets of more than $ 2 billion. The evolution of the biotechnology industry could be documented through the career of a specific scientist/entrepreneur, Alexander Zaffaroni. Working primarily in Silicon Valley, Zaffaroni's career has included creation of Syntex, a pharmaceutical/chemistry company, ALZA, a company producing delivery systems including the nicotine patch, DNAX, a research think-tank for Schering-Plough, and Affymatrix, a company representing the fundamental wedding of silicon valley with the biotechnology industry.

Pajaro Dunes Conference - Relationships Between Academia and Industry

In March 1982, the heads of five major research universities and eleven corporations met in California to contemplate the ramifications of academia's growing interest in collaborating with industry, particularly the biotechnology industry. Organized by the presidents of Stanford University, Harvard University, Massachusetts Institute of Technology, California Institute of Technology, and the University of California, academic faculty members and business representatives from companies including Genentech, Syntex, Gillette, DuPont, Eli Lilly, and Cetus attended the conference. While no firm policy decisions were reached, the conference initiated discussions on issues relevant to collaboration including contract disclosure, patents and licenses, and conflicts of interest.

Discovery and Patenting of PCR by Cetus and the inventor Kary Mullis

In 1985, a patent for PCR, the DNA polymerase chain reaction, was granted to Kary B. Mullis and assigned to the Cetus Corporation. This truly remarkable technique enables a tiny fragment of DNA to be amplified as much as a billionfold. For the immediate application of this technique to the diagnosis of disease, a license was granted by Cetus to Hoffmann-La Roche (Roche) virtually excluding other competitors in the diagnostics business from accessing this powerful technology. Lawyers for the Dupont Corporation argued that Kary Mullis's ideas were inspired packaging of a good idea and one deserving commercial advantage, but as with the rediscovery of the wheel, not a patentable invention, however a court of law found in favor of Cetus. After the verdict, Chiron purchased Cetus and sold the PCR patent portfolio to Roche for $ 300 million. Roche has usually denied industrial applicants who have sought licenses to use the PCR patent, resulting in many companies developing alternatives to circumvent the technique.[91]

Entrepreneurial Academic Scientist/Evolution of University/Industry Partnerships

In the mid-1970s, developments in recombinant DNA technologies made the basic research tenets of molecular biology commercially tenable overnight. Many academic scientists began to seek industrial means to develop the research ideas discovered in their university laboratories. However, the academic structure was not sufficiently prepared to immediately transfer these ideas to industrial settings for development. During the last twenty years, there has been a major shift in the attitudes of both university administrators and faculty towards academic scientists associating with corporate interests. The University of California, like other universities, has systemwide technology licensing offices, and the mechanisms are in place to protect patentable ideas produced in the academic setting. Further mechanisms to foster collaboration are being developed and the effects of industrial relationships on the academic setting continue to be explored.

Academic Foundation of Biotechnology Industry: UCB, UCSF , and Stanford

The University of California Berkeley, and the University of California San Francisco are two of the most historically connected campuses in the UC system. Once the medical center for the Berkeley campus, UCSF became a distinct campus in the mid-1960s. Since the merger of the San Francisco based Toland Medical School with the University of California, there has been a continual migration of the scientific research departments across the Bay and faculty from both Berkeley and San Francisco have contributed major discoveries in biomedicine. Simultaneously, Stanford University founded a medical school, became a force in biochemistry and genetics, and established an industrial park designed to enhance technology transfer. These three campuses have fostered the formation of the biotechnology industry in the Bay Area. An exploration of the roots of the basic sciences, university administration, and the social context of science at each of these campuses would provide insight into the development of the entrepreneurial scientist, examine the role of an academic medical center in biotech product development, and explore the importance of industry locale on the development of the biotechnology industry.

Impact of University/Industry Partnerships on Education of Students

---

[91]ibid. p. 236

Existing UC policies support a student's right to academic freedom and his or her right to academic guidance free from commercial considerations. With the growing involvement of industry on campuses in many and varied arrangements, a broader discussion of such influence on the general quality of the entire educational experience is appropriate. Some of the issues important to document include exploring the balance between practical employment-focused training and the investigation of fundamental questions, as well as the implications to students of the increasing amount of proprietary information in the midst of the UC research enterprise.[92]

Affymetrix: Intersection of Computers and Biology - The DNA Chip

In Silicon Valley, a group of technicians are assembling batches of chips with the usual machines of a semiconductor factory. However, these chips are not fabricated from layers of silicon, they are being made from DNA, and they are designed not to do computations but to read out the turbulent streams of information that evolution has packed into the genomes of living organisms. This striking intersection of biology and computers is being engineered at a company called Affymetrix which was founded by Alexander Zaffaroni. Prototype Affymetrix chips are already able to measure gene expression and to detect the mutation in certain genes that foster a disposition toward cancer.[93].

B. Documenting Specific Products Developed by Biotech Companies (see Appendix B)

Cetus
Chiron
Genentech

C. Collecting Specific Organizational Records (see Appendix C)

Academia
Industry

D. Preserving Individual Scientists Papers (see Appendix D)

UCB
UCSF
Stanford
Industry

E. Documenting Campus Laboratories and Research Centers (see Appendix E)

UCB

Proceedings of the President's Retreat. The University of California's Relationships with Industry in Research and Technology Transfer. January 30-31, 1997. p. 249.[92]

[93] New York Times, April 8, 1997

UCSF

F. Documenting Specific Companies (see Appendix F)
Chiron Absorbed Companies
Chiron Spinoffs
Genentech Spinoffs
Companies Stanford University could document

G. Capturing Oral History Interviews (see Appendix G)

3. Project Recommendations

A. *Improving Preservation of Scientific Research Records at Universities*

As part of the UC Biotechnology Collaboration Project, The Bancroft Library, UC Berkeley and the UCSF Library and CKM, Archives and Special Collections should implement and encourage support for the following:

1. Department Chairs should be contacted systematically to assist in the identification of significant and representative experiments, key faculty members, and principal investigators.

2. Professional files of these key faculty members should be preserved by the University Archives and Special Collections as appropriate (see Appraisal section for types of records to preserve).

3. A core set of records should be preserved by the University Archives and/or Special Collections at each campus to provide basic documentation of all experiments in molecular biology and related academic fields. These core records include the administrative files for the senior officer for research, for example at UCSF, the Vice Chancellor for Research Affairs; the annual reports for appropriate departments such as biochemistry, molecular and cellular biology, pharmaceutical chemistry, etc.; and summary administrative and financial information maintained by the Contracts and Grants Office which would reveal sources of external support, sums acquired and projects supported. This model assumes that University Libraries are maintaining access to electronic versions or physical copies of the peer review journals which provide an exhaustive description of disseminated research results.

4. Records generated by individual campus and UC systemwide committees concerned with conflict of interest, technology transfer, and university/industry relationships be preserved by appropriate University Archives. These records include meeting minutes, correspondence, and reports.

4. UC Archivists Council in conjunction with the UC Records Management Group should recommend to the UC Office of the President (UCOP) a review of the current UC Records Disposition Schedule (RDS) specifically addressing retention schedules for patent case files and patent financial records that are presently scheduled for destruction seven years after patent expiration. Recommend changing the UC RDS to ensure these files are reviewed by individual campus University Archivists for historical value prior to destruction.

5. UC Archivists Council in conjunction with the Electronic Records Work group, and the UC Records Management Group recommend to the UC Office of the President that a task force be formed to develop campus-appropriate systems for the appraisal, selection, and preservation of electronic mail (email) generated by research faculty and that retention schedules be developed for email as part of the UC Records Disposition Schedule.

6. UC Archivists Council in conjunction with the UC Records Management Group recommend to UCOP the formation of a task force comprised of campus scientific faculty, archivists, records managers, and legal counsel to develop a management system for scientific research notebooks to ensure their preservation.

B. *Strategies for Preserving the History of Biotech Companies*

Short Term Strategy One:
Encourage the Development of Archival/Oral History Programs at Chiron and Genentech

The UC Collaborative Biotechnology Project should engage the Chief Executive Officers at Chiron and Genentech in a dialogue stressing the importance of institutional memory to the continued success of their biotechnology ventures, and that history can best be preserved by archival and oral history programs. History is based upon surviving evidence, and this evidence takes the form of written documents, artifacts, and the recorded thoughts, ideas, and memories of living persons. Archival documents provide a record of what transpired, while oral histories provides a sense of how and why events transpired. Archival documents can also provide a check to the collective memory, while oral history provides a context to the produced paper documentation, and gives insight into experiences otherwise never recorded. Applied simultaneously, the preservation of historical archival materials, and the captured experiences of individuals provide a means of reconstructing significant past events. Many successful businesses including Hewlitt-Packard, Levi-Strauss Company, and the Wells Fargo Bank maintain archival and oral history programs which actively support the business goals of the companies. Archival and oral history programs support good business practices by preserving institutional memory which can assist in corporate planning, management development, marketing, legal support, public affairs and public relations. Corporations, like individuals, "benefit from the old ways of doing things, but may also become unable to adapt during periods of change. At these times, managers can look at the history of an organization to find ways it adapted in the past ..... history is also useful as a diagnostic tool and as a way ..... to motivate employees in the present. A company's history contains its heritage and traditions, which managers need to understand if they are to see the present as part of a process rather than a collection of happenings." [94]Finally, at Sandia National Laboratory, a program of video oral histories is available through the laboratory intranet providing an invaluable and accessible resource as well as a means of maintaining institutional memory when staffing levels change due to layoffs, retirements and the recruitment of new personnel.

Three recommendations should be made to the CEOs of Chiron and Genentech:

1. Professional archival programs should be initiated in conjunction with current on-going records management programs to ensure the preservation of valuable historical information.

2. Oral history programs should be initiated at the companies, coordinated and/or sponsored by the company archives and records management programs.

3. Microfilm annual reports/newsletters from Chiron & Genentech; originals maintained by companies and microfilm available for use at UC Berkeley and UC San Francisco manuscript repositories.

Short Term Strategy Two:
Preserve the Resources Compiled by the Bay Area Bioscience Center

[94]Smith, George David et al. "Present Value of Corporate History." Harvard Business Review, November-December 1981.

Supported by local biotechnology companies, the mission of the Bay Area Bioscience Center is to increase the public's understanding of the biosciences and their unique role in Northern California. Located in Oakland, the center sponsors programs that focus on public information, science education, employment issues, job searches and data collection. As such, the Bioscience Center collects, maintains, and serves as a centralized source of published information about the biotechnology industry in the San Francisco by maintaining reference files for individual companies. These reference files are used by persons seeking employment in the biotech industry, science writers and the general public, however these reference files will provide a good overall picture of the industry for scholarly research.

One recommendation should be made to the Director of the Bay Area Bioscience Center:

1. Microfilm the company subject files maintained by the Bioscience Center. The originals remain at Bioscience Center and the microfilm copies are available for research use at UC Berkeley and UC San Francisco manuscript repositories.

Short Term Strategy Three:
Encourage the Preservation of Biotechnology Historic Documents Maintained at Venture Capital Firms

1.The UC Collaborative Biotechnology Project should contact the Executive Directors at the venture capital firms that helped Chiron and Genentech develop their original business plans and first offerings of public stock. The purpose of these meetings will be to stress the importance of preserving the history of these two biotechnology companies, and to identify materials that should be preserved by the venture capital firm, the biotech companies, and appropriate university manuscript repositories.

Short Term Strategy Four:
Developing Relationships with Biotech Companies Founded by UC Faculty & Alumni

Exploring the linkages between universities and industry has been central to understanding the emergence of the biotechnology industry. Thus far the project has focused on Chiron and Genentech, the two prominant first generation biotechnology companies in the San Francisco Bay Region. The next step should be to increase awareness of the project and its goals by widening the circle of companies contacted to include the second generation of the biotechnology industry. Obvious candidates would include companies in the Bay Area founded by UC Berkeley or UC San Francisco faculty or alumni. Therefore:

1. The UC Collaborative Biotechnology Project should survey companies founded by UC Berkeley and UC San Francisco faculty or alumni to determine if records management programs are in operation, and contact the company CEOs with the intent of discussing the project goals and our willingness to make recommendations about establishing professional records management and archival programs at their companies. As appropriate, these discussions should initiate efforts to begin documenting the companies ephemerally by collecting and preserving annual reports and newsletters published by the company, and explore the possible long-term donation of company papers to the appropriate manuscript repositories at UC Berkeley and UC San Francisco.

The following list of companies was provided by the Critical Linkages Project sponsored by the UC Biotechnology Systemwide Office, and includes the names of companies founded by UCB and UCSF scientists or alumni as designated in the corporate documents:

AvMax, Inc. (So. SF, CA), founded by Dr. Benet, UCSF Faculty
Bio-Rad Laboratories, Inc. (Hercules, CA), founded by Dr. Schwartz, UCB Alumni
California Biotechnology Inc. (Mountain View, CA) founded by Dr. Baxter, UCSF Faculty
Genelabs Technologies, Inc. (Redwood City, CA) founded by Dr. Kung, UCB Alumni
Genetrace Systems, Inc. (Menlo Park, CA) founded by Dr. Becker, UCB Alumni
Glycomed, Inc. (Alameda, CA) founded by Dr. Klock, UCSF Faculty
Glyko, Inc. (Novato, CA) founded by Dr. Klock, UCSF Faculty
LXR Biotechnology, Inc. (Richmond, CA) founded by Dr. Barr, UCSF Faculty
Metra Biosystems, Inc. (Mountain View, CA) founded by Dr. Arnaud, UCSF Faculty
Prototek (Dublin, CA) founded Dr. Smith, UCSF Faculty
Scios, Inc. (Mountain View, CA) founded by Dr. Baxter, UCSF Faculty
Tularik, Inc. (So. SF, CA) founded by Dr. Tjian, UCB Faculty
Xoma (Berkeley, CA) founded by Dr. Scannon, UCSF Faculty

Long Term Strategy
Preserve the Administrative and Research Records of Chiron and Genentech

The UC Collaborative Biotechnology Project should maintain regular contact with the CEOs of Chiron and Genentech to develop lasting partnerships to foster the eventual transfer of their permanent historical corporate records to the archival and manuscript repositories at UC Berkeley and UC San Francisco. The nature of proprietary information prevents the preservation of these corporate records at University of California archival repositories in the near future.

Observations by Biotechnology Industry Personnel

In discussing the role that University Archives and Special Collection repositories might take in encouraging the preservation of historical information at Chiron, Martha Truett, Chief Forensic Scientist and Manager of Legal Information Systems, noted "that the issue of confidentiality for Chiron newsletters and other documents detailing work at Chiron would be an issue requiring resolution before University preservation of our documents could be considered."[95] Irene Loeffler, Manager of Records and Image Systems at Genentech stated that "Corporate Communications keeps the annual reports and newsletters for the company, and it would be appropriate to approach them about microfilming these ephemeral documents for the libraries."[96]

C. *Formulating Documentation Partnership with Stanford University*

The Stanford University Libraries would make an excellent partner for the documentation of biotechnology in the Bay Area. Stanford faculty have made significant contributions to the development of recombinant DNA technologies, the campus has close proximity to Silicon Valley and its growing number of biotechnology companies (see Appendix for list of companies nearby to Stanford University), and the Libraries have an extensive track record collecting published and unpublished materials concerning the history of science and technology.

The Stanford University Libraries have collected seminal published works in science, such as the Samuel I. and Cecil M. Barchas Collection in the History of Science and Ideas, the Stephen P. Timoshenko Collection in the History of Mechanics, and the Frederick E. Brasch Collection on Sir Isaac Newton and the History of Scientific Thought, as well as sizable retrospective holdings of monographs, journals, and technical reports in the sciences and engineering. The University Archives contains many manuscript collections in the history of

---

[95]Interview Truett with Chandler
[96]Interview Loeffler with Chandler

science and technology, emphasizing the fields in which Stanford has played a prominent role ranging from high energy physics and microelectronics to earth sciences and population biology.

Working with Stanford's History of Science Program, and the Program in Values, Technology, Science and Society, the Stanford University Libraries have an established formal program to document the history of science and technology at Stanford and in the Silicon Valley. Since World War II, there has been a rapid growth of high-technology industries around Stanford University. Academic strengths in science and engineering culminated in the invention of the klystron, which produces microwave energy and fostered the creation of the Silicon Valley industries which have resulted in developments including the laser, the microprocessor, and discoveries in high-energy physics as well as contributions to the field of biotechnology. The close proximity of the Stanford Industrial Park has fostered this fruitful flow of ideas between industry and academia. With the *Stanford and the Silicon Valley Project* , the Stanford University Libraries are seeking to identify and preserve original papers and manuscripts crucial to understanding the process of discovery, innovation, and product development. In addition, the Stanford University Archives currently maintains collections of professional papers donated by faculty members Arthur Kornberg and Paul Berg whose discoveries helped establish recombinant DNA technology.

Coordinated by Tim Lenoir, Historian of Science, and Henry Lowood, Bibliographer in the History of Science, the Stanford University Libraries are actively participating in the technological development of *HoTNet: A History of Technology Network* funded by the Alfred P. Sloan Foundation. The project will establish a network of History of Technology Websites documenting The New York Blackouts, developed by James Sparrow of Brown University; The Computer Mouse, developed by Tim Lenoir of Stanford University; The Boston Central Artery/Tunnel Project, developed by Thomas P. Hughes of MIT; Polymerase Chain Reaction (PCR) developed by Paul Rabinow of UC Berkeley; and Electric Vehicle Drivers and Owners, developed by David A. Kirsch of UCLA. Beginning in 1997, this two-year project will explore the means by which internet-based technologies can offer scholars an exciting new environment in which to author works and to learn. By digitizing primary source materials and archival documents, the project scholars seek to construct flexible on-line resources that will grow in accordance with the needs of users.

In May of 1997, I met with Maggie Kimball, Stanford University Archivist, and Henry Lowood to discuss the UC Berkeley and UC San Francisco collaborative effort to document biotechnology in the Bay Area. Speaking from experience, Lowood noted that it had been difficult to document companies in the Silicon Valley. However, both Kimball and Lowood agreed that they would be willing to pursue collecting the administrative papers created at Stanford University during the development of the Cohen/Boyer patent. Lowood commented that *Science* covered issues surrounding the development of the Cohen/Boyer patent extensively during the 1970s. Because of the difficulty he has experienced in documenting private companies, Lowood believes a good initial strategy for documenting the industry is producing a bibliography citing the scientific literature on patents and he further commented that in general, "companies could be documented ephemerally by preserving newsletter articles concerning patents."[97]

D. *Biotechnology Documentation Effort By the Libraries of UC Berkeley and UC San Francisco*

As part of the UC Biotechnology Collaboration Project The Bancroft Library, UC Berkeley and the UCSF Library & CKM, Archives and Special Collections should implement the following recommendations:

1. In conjunction with the Stanford University Libraries, The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections should identify and collect published and unpublished materials which will document these significant topics (explained earlier in detail):

-Development of the NIH Guidelines on Genetic Engineering - Asilomar Conference
-Foundation of Recombinant DNA Technologies
-Discovery of Recombinant DNA and the Cohen-Boyer Patent by Stanford/UC
-Race for Insulin
-Pajaro Dunes Conference -Relationships Between Academia and Industry
-Entrepreneurial Academic Scientist/Evolution of University/Industry Partnerships
-Academic Foundation of Biotechnology Industry: UCB, UCSF and Stanford
-Impact of University/Industry Partnerships on Education of Students

2. The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections should collect and preserve specific organizational records pertanent to research in molecular biology and the

[97]Interview Lowood with Chandler 5/20/97

biotechnology industry produced by the University of California and its campuses. These include:

-Data sets of California biotech industry UC faculty and alumni, UC Biotech Systemwide Office
-Informal Reports, UC Biotech Systemwide Office
-Records of the UCOP Office of Technology Transfer
-Records of the UCB Office of Technology Licensing
-Meeting Minutes, UCB Conflict of Interest Committee
-Records of the UCSF Legal Support Services
-Records of the UCSF Office of Research Affairs
-Records of the UCSF Office of Technology Management
-Meeting Minutes, UCSF Conflict of Interest Committee
-Meeting Minutes, UCSF University-Industry Relations Committee
(See Appendix C for a complete listing)

3. The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections should preserve the papers of their campus specific scientific faculty and the papers of major industry figures who have made significant contributions in the field of molecular biology and related disciplines, as well as to the development of the biotechnology industry. See Appendix D for a complete listing of suggested faculty and industry scientists to document. UC Berkeley and UC San Francisco should also encourage the Stanford University Libraries in the collection of relevent faculty papers.

4. The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections should survey and identify records relevant to the documentation of biotechnology at relevant campus laboratories and research centers. See Appendix E for a complete listing.

5. By encouraging the development of archival and oral history programs at local biotechnology companies, The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections will indirectly assist with the documentation of significant topics, specific products and companies including:

Signficant Topics:

-Race for Insulin
-Creation and Evolution of the Biotechnology Industry
-Discovery and Patenting of PCR by Cetus
-Affymetrix: Intersection of Computers and Biology - The DNA Chip

Specific Products created by Cetus, Chiron and Genentech

Specific Companies absorbed by and spunoff from Chiron and Genentech

(See Appendices for complete listings)

6. The Bancroft Library, UC Berkeley and the UC San Francisco Library and CKM, Archives and Special Collections should support academic research and science education programs and foster longterm public understanding of molecular biology and biotechnology by promoting access and public awareness. The UC Biotechnology Collaboration Project can engender this kind of use by creating online scholarly research and public access tools about biotechnology. Appropriately, this project should develop a website devoted to Biotechnology in the Bay Area with links to EAD finding aids for relevant UC Library archival and manuscript collections, develop biotechnology oral histories on the internet, create links to local biotechnology companies online, share resources with *HoTNet: A History of Technology Network* , and support the development of online educational tools including biotechnology exhibits and virtual scientific conferences.

IV. UC Biotechnology Collaboration Project Business Model

A formally established UC Biotechnology Collaboration Project would serve as a regional resource to support the preservation of the history of the development of biotechnology within the San Francisco Bay Area focusing on academic research programs in molecular biology, the development of the biotechnology industry and the critical linkages between universities, industry, and the government. To implement this Project, it is necessary to develop a business plan and suggest possible funding sources. This Collaboration will best be served by hiring a Project Archivist for a three-year grant funded project who will work 50% time at The Bancroft Library, UC Berkeley and 50% time at the UCSF Library & CKM, Archives & Special Collections under the respective supervision of the Curator for the History of Science and Technology at The Bancroft Library, and the Head of Archives and Special Collections at the UCSF Library & CKM. These efforts will be coordinated with The Bancroft Library's Biotechnology Oral History Program.

<u>1. Business Plan: Implementing the Project Recommendations</u>

A. Workplan

<u>1. Hire Project Archivist:</u> Individual has previous experience managing an archival project including administration, processing, and reference. Specific skills include project design and planning, donor negotiations, appraisal,

processing, supervision , SGML encoding of finding aids and website development.

2. Coordinate Advisory Personnel: Biotechnology Advisory Boards at UC Berkeley and UC San Francisco will assist the Project Archivist in prioritizing and clarifying the issues and activities to document and advise on the establishment of policies governing access. The Boards represents individuals involved in molecular biology research, the biotechnology industry, and scholarly research who are familiar with persons of significance and their activities, can assist with contacting individuals or companies groups who should be documented, and can serve as contacts to project funding sources.

3. Implementation of Project Recommendation A: To Improve the Preservation of Scientific Research Records at UC Berkeley and UC San Francisco, the Project Archivist will contact Department Chairs at UC Berkeley and UC San Francisco to begin to identify key faculty members whose papers should be preserved, identify and preserve the core records for documenting molecular biology research, identify and preserve files generated by campus offices concerned with technology transfer and conflicts of interest, and working with the University Archivist at UC Berkeley and the Head of Archives & Special Collections at UC San Francisco, draft recommendations to the UC Archivists Council concerning retention of patent files and electronic mail, as well as scientific notebook management.

4. Implementation of Project Recommendation B: Working closely with the Head of Archives and Special Collections at UCSF, the Project Archivist will begin to implement the Strategies for Preserving the History of Biotech Companies. The Project Archivist will arrange meetings with the CEOs at Chiron and Genentech to discuss the development of Archival/Oral History Programs at those companies; draft a funding proposal for microfilming the company reference files maintained at the Bay Area Bioscience Center; arrange meetings with the Executive Directors of specific venture capital firms to encourage the preservation of historic biotechnology records; and survey biotech companies established by UC faculty and alumni for the existance of records management programs and informing these companies about the collaborative project.

5. Implementation of Project Recommendation C: Working closely with the Director of The Bancroft Library, the UCSF University Librarian, and the Head of Archives and Special Collections at UCSF, the Project Archivist will help coordinate the formation of a biotechnology documentation partnership with the Stanford University Libraries.

6. Begin Implementation of Project Recommendation D: Biotechnology Documentation Effort By the Libraries of UC Berkeley and UC San Francisco. Working closely with the Head of Archives and Special Collections at UCSF, the Project Archivist will identify and define the specific groups and individuals whose papers should be examined, these include significant biotechnology topics, organizational records at UC campuses, specific scientists, and relevant UC campus laboratories and research centers. In addition, the Project Archivist will identify relevant published sources of information worthy of preservation. Agencies and individuals are contacted, goals of project are explained and the importance of their participation. Discuss arrangements for future transfer of materials and their ultimate use by researchers.

7. Survey Papers and Records: Using a questionnaire which records data, determine organizational history, including mission and functions, determine types and amounts of available records, physical condition and legal status (ownership, confidentiality restrictions).

8. Accession and Process Papers and Records: Assemble necessary transfer of ownership papers and arrange for transfer of collections to The Bancroft Library and the UCSF Library for processing. Receive and process records at both repositories as appropriate. Determine physical condition, remove irrelevant materials, damaging items (paper clips, rubber bands, etc.), organize and arrange according to accepted archival practice (in original order, if logical or by series (types of materials -- correspondence, meeting minutes, etc.) and/or by chronology; rehouse in acid-free folders, boxes and cartons to prevent deterioration.

9. Create Public Access to Papers and Records: Create SGML encoded finding aids for collections: describe organizational history, scope and content note, and create record group inventories (lists of contents in series by folder); make finding aids available through the Biotechnology Project website; create records in statewide and national cataloging databases (OCLC or RLIN, largest national databases of cataloged materials which make information available in the University of California's MELVYL system); shelve collections in high security, environmental controlled storage areas.

10. Publicize Availability of Biotechnology Collections: The Project Archivist will develop a website devoted to Biotechnology in the Bay Area with links to EAD finding aids at The Bancroft Library, UC Berkeley and the UCSF Library & CKM, Archives and Special Collections and other relevant UC Library archival and manuscript collections. The Project Archivist will also work with UC Berkeley ROHO staff to make links to online biotechnology oral histories as they are developed. Links will be established to local biotechnology companies' websites

as well, and other relevant electronic resources. Physical access will be provided to the materials in secure environments at The Bancroft Library, UC Berkeley reading room and the UCSF Library Archives and Special Collections reading room, where papers are used under the supervision of staff and materials are copied on request.